******* QUERY RESULTS *******

```
=> d his l36

     (FILE 'HCAPLUS' ENTERED AT 16:42:06 ON 10 JUL 2007)
L36          10 S L25 OR L33 OR L34

=> d que l36
L2           27 SEA FILE=REGISTRY ABB=ON  PLU=ON  (10043-66-0/BI OR 10098-91-6/
                BI OR 23214-92-8/BI OR 50-18-0/BI OR 57-22-7/BI OR 10043-49-9/B
                I OR 11056-06-7/BI OR 14265-85-1/BI OR 14378-26-8/BI OR
                14596-37-3/BI OR 14998-63-1/BI OR 154-93-8/BI OR 15755-17-6/BI
                OR 15755-39-2/BI OR 15757-86-5/BI OR 15776-20-2/BI OR 33419-42-
                0/BI OR 4346-18-3/BI OR 50-02-2/BI OR 50-24-8/BI OR 53-03-2/BI
                OR 58-05-9/BI OR 59-05-2/BI OR 671-16-9/BI OR 83314-01-6/BI OR
                83869-56-1/BI OR 9001-99-4/BI)
L4              QUE  ABB=ON  PLU=ON  (ANTIGENS (2A) (CD20 OR CD(W)20)) OR
                 (ANTI (2A)(CD20 OR CD(W)20))
L5              QUE  ABB=ON  PLU=ON  (ANTIGENS (2A) (CD74 OR CD 74)) OR (
                ANTI (2A) (CD74 OR CD(W)74))
L6              QUE  ABB=ON  PLU=ON  (HLA DR (2A) ANTIGENS) OR HDA DR
L7              QUE  ABB=ON  PLU=ON  NAKED ANTIBODIES OR NAKED ANTIBODY
L11             QUE  ABB=ON  PLU=ON  IMMUNOTHERAP?
L14      139742 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2
L15          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RADIOLABEL? IMMUNOCONJUGATE?/O
                BI
L16      256904 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CYTOKINE/OBI OR TOXIN/OBI OR
                FUSION PROTEIN/OBI OR RNASE/OBI OR RECOMBIN? RNASE/OBI OR
                RIBONUCLEASES/OBI
L17      374269 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L14 OR L15 OR L16)
L18        7247 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L4 OR L5 OR L6 OR L7)
L19      204919 SEA FILE=HCAPLUS ABB=ON  PLU=ON  B CELL/OBI OR T CELL/OBI OR
                MYELOID CELL/OBI OR MAST CELL/OBI OR PLASMA CELL/OBI
L20      316123 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SHEEP/OBI OR GOAT/OBI OR
                HORSE/OBI OR CATTLE/OBI OR ALPACA/OBI OR PIG/OBI OR DOG/OBI OR
                CAT/OBI
L21        1953 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 (L) L20
L22         286 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21 AND (L17 OR L18)
L23      761994 SEA FILE=HCAPLUS ABB=ON  PLU=ON  15/SX,SC
L24         248 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22 AND L23
L25           9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24 AND L11
L26             QUE  ABB=ON  PLU=ON  B CELL
L28             QUE  ABB=ON  PLU=ON  AY<2003 OR PRY<2003 OR PY<2003 OR MY
                <2003 OR REVIEW/DT
L30          49 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24 AND L26
L32          39 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30 AND L28
L33           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 AND L14
L34           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 AND L11
L36          10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 OR L33 OR L34


=> d his l46

     (FILE 'WPIX' ENTERED AT 16:56:33 ON 10 JUL 2007)
L46           9 S L44 AND L27

=> d que l46
L2           27 SEA FILE=REGISTRY ABB=ON  PLU=ON  (10043-66-0/BI OR 10098-91-6/
                BI OR 23214-92-8/BI OR 50-18-0/BI OR 57-22-7/BI OR 10043-49-9/B
                I OR 11056-06-7/BI OR 14265-85-1/BI OR 14378-26-8/BI OR
                14596-37-3/BI OR 14998-63-1/BI OR 154-93-8/BI OR 15755-17-6/BI
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                OR 15755-39-2/BI OR 15757-86-5/BI OR 15776-20-2/BI OR 33419-42-
                0/BI OR 4346-18-3/BI OR 50-02-2/BI OR 50-24-8/BI OR 53-03-2/BI
                OR 58-05-9/BI OR 59-05-2/BI OR 671-16-9/BI OR 83314-01-6/BI OR
                83869-56-1/BI OR 9001-99-4/BI)
L4              QUE  ABB=ON  PLU=ON  (ANTIGENS (2A) (CD20 OR CD(W)20)) OR
                 (ANTI (2A)(CD20 OR CD(W)20))
L5              QUE  ABB=ON  PLU=ON  (ANTIGENS (2A) (CD74 OR CD 74)) OR (
                ANTI (2A) (CD74 OR CD(W)74))
L6              QUE  ABB=ON  PLU=ON  (HLA DR (2A) ANTIGENS) OR HDA DR
L7              QUE  ABB=ON  PLU=ON  NAKED ANTIBODIES OR NAKED ANTIBODY
L11             QUE  ABB=ON  PLU=ON  IMMUNOTHERAP?
L14      139742 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2
L15          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RADIOLABEL? IMMUNOCONJUGATE?/O
                BI
L16      256904 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CYTOKINE/OBI OR TOXIN/OBI OR
                FUSION PROTEIN/OBI OR RNASE/OBI OR RECOMBIN? RNASE/OBI OR
                RIBONUCLEASES/OBI
L17      374269 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L14 OR L15 OR L16)
L18        7247 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L4 OR L5 OR L6 OR L7)
L19      204919 SEA FILE=HCAPLUS ABB=ON  PLU=ON  B CELL/OBI OR T CELL/OBI OR
                MYELOID CELL/OBI OR MAST CELL/OBI OR PLASMA CELL/OBI
L20      316123 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SHEEP/OBI OR GOAT/OBI OR
                HORSE/OBI OR CATTLE/OBI OR ALPACA/OBI OR PIG/OBI OR DOG/OBI OR
                CAT/OBI
L21        1953 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 (L) L20
L27             QUE  ABB=ON  PLU=ON  AY<2003 OR PY<2003 OR PRY<2003
L43         339 SEA FILE=WPIX ABB=ON  PLU=ON  L21 AND (L17 OR L18)
L44          19 SEA FILE=WPIX ABB=ON  PLU=ON  L43 AND L11
L46           9 SEA FILE=WPIX ABB=ON  PLU=ON  L44 AND L27


=> d his l57

     (FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, DRUGU, PASCAL' ENTERED AT
     17:04:51 ON 10 JUL 2007)
L57          19 S L56 AND L28

=> d que l57
L2           27 SEA FILE=REGISTRY ABB=ON  PLU=ON  (10043-66-0/BI OR 10098-91-6/
                BI OR 23214-92-8/BI OR 50-18-0/BI OR 57-22-7/BI OR 10043-49-9/B
                I OR 11056-06-7/BI OR 14265-85-1/BI OR 14378-26-8/BI OR
                14596-37-3/BI OR 14998-63-1/BI OR 154-93-8/BI OR 15755-17-6/BI
                OR 15755-39-2/BI OR 15757-86-5/BI OR 15776-20-2/BI OR 33419-42-
                0/BI OR 4346-18-3/BI OR 50-02-2/BI OR 50-24-8/BI OR 53-03-2/BI
                OR 58-05-9/BI OR 59-05-2/BI OR 671-16-9/BI OR 83314-01-6/BI OR
                83869-56-1/BI OR 9001-99-4/BI)
L4              QUE  ABB=ON  PLU=ON  (ANTIGENS (2A) (CD20 OR CD(W)20)) OR
                 (ANTI (2A)(CD20 OR CD(W)20))
L5              QUE  ABB=ON  PLU=ON  (ANTIGENS (2A) (CD74 OR CD 74)) OR (
                ANTI (2A) (CD74 OR CD(W)74))
L6              QUE  ABB=ON  PLU=ON  (HLA DR (2A) ANTIGENS) OR HDA DR
L7              QUE  ABB=ON  PLU=ON  NAKED ANTIBODIES OR NAKED ANTIBODY
L8              QUE  ABB=ON  PLU=ON  SHEEP OR GOAT OR HORSE OR CATTLE OR
                ALPACA OR PIG OR DOG OR CAT
L11             QUE  ABB=ON  PLU=ON  IMMUNOTHERAP?
L13             QUE  ABB=ON  PLU=ON  (DOMESTIC OR COMPANION) (2A) (ANIMAL
                )
L14      139742 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2
L15          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RADIOLABEL? IMMUNOCONJUGATE?/O
                BI
```

```
L16      256904 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CYTOKINE/OBI OR TOXIN/OBI OR
                FUSION PROTEIN/OBI OR RNASE/OBI OR RECOMBIN? RNASE/OBI OR
                RIBONUCLEASES/OBI
L17      374269 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L14 OR L15 OR L16)
L18        7247 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L4 OR L5 OR L6 OR L7)
L19      204919 SEA FILE=HCAPLUS ABB=ON  PLU=ON  B CELL/OBI OR T CELL/OBI OR
                MYELOID CELL/OBI OR MAST CELL/OBI OR PLASMA CELL/OBI
L20      316123 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SHEEP/OBI OR GOAT/OBI OR
                HORSE/OBI OR CATTLE/OBI OR ALPACA/OBI OR PIG/OBI OR DOG/OBI OR
                CAT/OBI
L21        1953 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 (L) L20
L22         286 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21 AND (L17 OR L18)
L26             QUE  ABB=ON  PLU=ON  B CELL
L28             QUE  ABB=ON  PLU=ON  AY<2003 OR PRY<2003 OR PY<2003 OR MY
                <2003 OR REVIEW/DT
L52        4293 SEA L22
L53         164 SEA L52 AND L11
L55         164 SEA L53 AND (L8 OR L13)
L56          21 SEA L55 AND L26
L57          19 SEA L56 AND L28


=> dup rem l36 l46 l57
FILE 'HCAPLUS' ENTERED AT 17:29:31 ON 10 JUL 2007
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PROCESSING COMPLETED FOR L36
PROCESSING COMPLETED FOR L46
PROCESSING COMPLETED FOR L57
L69           32 DUP REM L36 L46 L57 (6 DUPLICATES REMOVED)
                 ANSWERS '1-10' FROM FILE HCAPLUS
                 ANSWERS '11-19' FROM FILE WPIX
                 ANSWERS '20-26' FROM FILE MEDLINE
                 ANSWERS '27-28' FROM FILE BIOSIS
                 ANSWER '29' FROM FILE EMBASE
                 ANSWERS '30-32' FROM FILE DRUGU

=> d l69 1-10 ibib ed abs hitind

L69  ANSWER 1 OF 32  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:564570  HCAPLUS  Full-text
DOCUMENT NUMBER:          147:2556
```

TITLE: Screening of Rec168 agonists or antagonists capable of inhibiting degranulation reaction or prostaglandin D2 production in mast cells for use as therapeutic agent against inflammation, autoimmune disease and allergy

INVENTOR(S): Tatemoto, Kazuhiko; Naito, Takayuki; Nozaki, Yuko; Furuno, Masahiro; Tomura, Keiko

PATENT ASSIGNEE(S): Japan Tobacco Inc., Japan; National University Corporation Gunma University

SOURCE: PCT Int. Appl., 144pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2007058336 | A1 | 20070524 | WO 2006-JP323063 | 20061114 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2005-330339 A 20051115

ED Entered STN: 25 May 2007

AB The object is to provide: a method for screening a substance capable of regulating degranulation or inhibiting prostaglandin D2 production; and a method for identification of a substance capable of inhibiting the degranulation or prostaglandin D2 production in a mast cell, these methods being useful for developing a therapeutic agent for an allergic disease or an autoimmune disease based on a new mechanism through a G protein-coupled receptor Rec168 (or MrgX2). Disclosed is a method for screening of a substance capable of inhibiting the signal transduction capability or a substance capable of regulating the degranulation or inhibiting the prostaglandin D2 production in a mast cell through Rec168. The method comprises the steps of: determining the signal transduction capability of a ligand having a Rec168-agonistic activity toward Rec168 in the presence or absence of a substance to be tested; and comparing a measurement value obtained in the presence of the substance with a measurement value obtained in the absence of the substance. Also disclosed is a method for identification of a substance capable of inhibiting the degranulation or prostaglandin D2 production in a mast cell.

CC 2-1 (Mammalian Hormones)
Section cross-reference(s): 1, 9, 15, 63

IT Cytokines
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(MBP (major basic protein); screening of Rec168 agonists, antagonists and antibodies capable of inhibiting degranulation reaction or prostaglandin D2 production in mast cells for use as therapeutic agent against inflammation, autoimmune disease and allergy)

IT Cytokines

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(histamine-releasing factor, peptides; screening of Rec168 agonists, antagonists and antibodies capable of inhibiting degranulation reaction or prostaglandin D2 production in mast cells for use as therapeutic agent against inflammation, autoimmune disease and allergy)

IT Allergy
Allergy inhibitors
Anti-inflammatory agents
Autoimmune disease
Cell degranulation
Drug screening
Human
Immunohistochemistry
Immunomodulators
Immunosuppressants
Immunotherapy
Inflammation
Mast cell
Molecular cloning
Protein sequences
Signal transduction, biological
cDNA sequences
(screening of Rec168 agonists, antagonists and antibodies capable of inhibiting degranulation reaction or prostaglandin D2 production in mast cells for use as therapeutic agent against inflammation, autoimmune disease and allergy)

IT 58-82-2, Bradykinin 33507-63-0, Substance P 38916-34-6, Somatostatin (sheep) 40077-57-4, Vasoactive intestinal octacosapeptide (swine) 53749-60-3, 4-11-Substance P 55508-42-4 64704-41-2, Granuliberin R 73032-94-7, Somatostatin-28 (sheep) 82989-21-7 86917-57-9 88898-17-3, Atrial natriuretic peptide-28 (rat) 89430-37-5 89430-38-6 108433-95-0, Magainin II 113294-82-9 115966-68-2 117992-65-1 119953-28-5 127317-03-7 136134-68-4 140896-21-5 302545-26-2 412961-36-5 937030-99-4 937031-00-0 937031-01-1 937031-02-2 937031-12-4 937719-25-0 937719-26-1 937719-27-2 937719-28-3 937719-29-4 937719-30-7 937719-31-8 937766-08-0
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(screening of Rec168 agonists, antagonists and antibodies capable of inhibiting degranulation reaction or prostaglandin D2 production in mast cells for use as therapeutic agent against inflammation, autoimmune disease and allergy)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 2 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:343970 HCAPLUS Full-text
DOCUMENT NUMBER: 144:389120
TITLE: Anti-human IRTA2 antibodies and conjugates for diagnosis and treatment of B cell malignancies
INVENTOR(S): Pastan, Ira H.; Ise, Tomoko; Xiang, Laiman; Nagata, Satoshi
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006039238 | A2 | 20060413 | WO 2005-US34444 | 20050922 |
| WO 2006039238 | A3 | 20070125 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-615406P P 20040930

ED Entered STN: 14 Apr 2006

AB Antibodies that specifically bind the extracellular domain of IRTA2 are disclosed herein. In one embodiment, these antibodies do not specifically bind IRTA1, IRTA3, IRTA4, or IRTA5. In one example, the antibodies are humanized antibodies. The antibodies can be conjugated to effector mols., including detectable labels, radionucleotides, toxins and chemotherapeutic agents. The antibodies that specifically bind IRTA2 are of use to detect B cell malignancies, such as hairy cell leukemia and non-Hodgkin's lymphoma. These antibodies that specifically bind IRTA2 are also of use to treat B cell malignancies that express IRTA2, such as hairy cell leukemia and non-Hodgkin's lymphoma.

IC ICM A61K

CC 15-3 (Immunochemistry)
Section cross-reference(s): 1, 3, 9, 63

ST human IRTA2 antibody conjugate immunodiagnosis immunotherapy B cell malignancy

IT Antitumor agents
Blood
Blood analysis
Blood plasma
Blood serum
DNA sequences
Drug delivery systems
Drugs
Epitopes
Fluorescence immunoassay
Genetic vectors
Hairy cell leukemia
Human
Immunotherapy
Molecular cloning
Mus musculus
Protein sequences
Test kits
(anti-human IRTA2 antibodies and conjugates for diagnosis and treatment of B cell malignancies)

IT Fusion proteins (chimeric proteins)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)

(anti-human IRTA2 antibodies and conjugates for diagnosis and treatment of B cell malignancies)

IT Abrins
Nucleic acids
Toxins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-human IRTA2 antibodies and conjugates for diagnosis and treatment of B cell malignancies)

IT Toxins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diphtheria, conjugates, antibody; anti-human IRTA2 antibodies and conjugates for diagnosis and treatment of B cell malignancies)

IT Toxins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diphtheria; anti-human IRTA2 antibodies and conjugates for diagnosis and treatment of B cell malignancies)

IT 9003-99-0, Peroxidase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(horse radish; anti-human IRTA2 antibodies and conjugates for diagnosis and treatment of B cell malignancies)

L69 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:974594 HCAPLUS Full-text
DOCUMENT NUMBER: 143:265323
TITLE: T Cell Epitope-Containing Peptides of the Major Dog Allergen Can f 1 as Candidates for Allergen Immunotherapy
AUTHOR(S): Immonen, Anu; Farci, Sandrine; Taivainen, Antti; Partanen, Jukka; Pouvelle-Moratille, Sandra; Naervaenen, Ale; Kinnunen, Tuure; Saarelainen, Soili; Rytkoenen-Nissinen, Marja; Maillere, Bernard; Virtanen, Tuomas
CORPORATE SOURCE: Department of Clinical Microbiology, University of Kuopio, Kuopio, Finland
SOURCE: Journal of Immunology (2005), 175(6), 3614-3620
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 08 Sep 2005
AB One prerequisite for developing peptide-based allergen immunotherapy is knowing the T cell epitopes of an allergen. In this study, human T cell reactivity against the major dog allergen Can f 1 was investigated to determine peptides suitable for immunotherapy. Seven T cell epitope regions (A-G) were found in Can f 1 with specific T cell lines and clones. The localization of the epitope regions shows similarities with those of the epitopes found in Bos d 2 and Rat n 1. On average, individuals recognized three epitopes in Can f 1. The results suggest that seven 16-mer peptides (p15-30, p33-48, p49-64, p73-88, p107-122, p123-138, and p141-156), each from one of the epitope regions, show widespread T cell reactivity in the population studied, and they bind efficiently to seven HLA-DRB1 mols. (DRB1*0101, DRB1*0301, DRB1*0401, DRB1*0701, DRB1*1101, DRB1*1301, and DRB1*1501) predominant in Caucasian populations. Therefore, these peptides are potential candidates for immunotherapy of dog allergy.
CC 15-9 (Immunochemistry)
ST T cell epitope dog allergen

immunotherapy
IT Allergens
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(Can f 1; epitope mapping for T-cells to major dog allergen)
IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA-DR; epitope mapping for T-cells to major dog allergen)
IT Immunotherapy
(desensitization; epitope mapping for T-cells to major dog allergen in relation to)
IT CD4-positive T cell
Canis familiaris
Human
Human groups
T cell (lymphocyte)
(epitope mapping for T-cells to major dog allergen)
IT Peptides, biological studies
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(epitope mapping for T-cells to major dog allergen)
IT Epitopes
(for T-cells to major dog allergen)
IT 863880-53-9 863880-54-0 863880-55-1 863880-56-2 863880-57-3 863880-58-4 863880-59-5
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(epitope mapping for T-cells to major dog allergen)
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 4 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:252369 HCAPLUS Full-text
DOCUMENT NUMBER: 140:269531
TITLE: Autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss in human and animal
INVENTOR(S): Boving, Tine Elisabeth Gottschalk; Klysner, Steen
PATENT ASSIGNEE(S): Pharmexa A/s, Den.
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004024183 | A1 | 20040325 | WO 2003-DK592 | 20030912 <-- |
| WO 2004024183 | B1 | 20040513 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,

OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| CA 2498739 | A1 | 20040325 | CA 2003-2498739 | | 20030912 <-- |
| AU 2003263150 | A1 | 20040430 | AU 2003-263150 | | 20030912 <-- |
| EP 1539232 | A1 | 20050615 | EP 2003-794825 | | 20030912 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| CN 1694724 | A | 20051109 | CN 2003-825086 | | 20030912 <-- |
| JP 2006504413 | T | 20060209 | JP 2004-535024 | | 20030912 <-- |
| IN 2005KN00485 | A | 20060623 | IN 2005-KN485 | | 20050323 <-- |
| NO 2005001779 | A | 20050411 | NO 2005-1779 | | 20050411 <-- |
| ZA 2005002929 | A | 20060222 | ZA 2005-2929 | | 20050411 <-- |
| PRIORITY APPLN. INFO.: | | | DK 2002-1345 | A | 20020912 <-- |
| | | | US 2002-410164P | P | 20020912 <-- |
| | | | WO 2003-DK592 | W | 20030912 |

ED Entered STN: 26 Mar 2004

AB Disclosed are novel methods that generally rely on immunization against autologous ghrelin. Immunization is preferably effected by administration of analogs of autologous ghrelin, said analogs being capable of inducing antibody production against the autologous ghrelin polypeptides. Especially preferred as an immunogen is autologous ghrelin, which has been modified by introduction of one single or a few foreign, immunodominant and promiscuous T-cell epitopes. Also disclosed are nucleic acid vaccination against ghrelin and vaccination using live vaccines as well as methods and means useful for the vaccination. Such methods and means include methods for the preparation of analogs and pharmaceutical formulations, as well as nucleic acid fragments, vectors, transformed cells, polypeptides and pharmaceutical formulations.

IC ICM A61K039-39
ICS A61K039-385; A61K039-00; C07K014-435; A61P003-04

CC 15-2 (Immunochemistry)
Section cross-reference(s): 3, 63

IT Amide group
Animal cell
Animal cell line
Animals
Anorexia
Antigen presentation
Antigen-presenting cell
Bos taurus
Burn
Cachexia
Canis familiaris
DNA sequences
Epitopes
Eubacteria
Eukaryota
Fungi
Genetic vectors
Human
Immunostimulants
Immunotherapy
Influenza virus
Microorganism
Molecular cloning
Mus
Obesity

PCR (polymerase chain reaction)
Plant cell
Plasmodium falciparum
Prokaryota
Protein sequences
Protozoa
Rattus
Sterculia urens
Sus scrofa domestica
Viral vectors
Wound
Yeast
cDNA sequences
(autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

IT Calreticulin
Carbohydrates, biological studies
Cytokines
DNA
Fluoropolymers, biological studies
Gelatins, biological studies
Gene
Haptens
Heat-shock proteins
Interleukin 1
Interleukin 12
Interleukin 13
Interleukin 15
Interleukin 2
Interleukin 4
Interleukin 6
Leader peptides
Lipids, biological studies
Polyanhydrides
Polysaccharides, biological studies
Polysiloxanes, biological studies
Polysiloxanes, biological studies
Polyurethanes, biological studies
Promoter (genetic element)
Receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

IT B cell (lymphocyte)
T cell (lymphocyte)
(epitope; autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

IT Fusion proteins (chimeric proteins)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ghrelin-T cell epitope; autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(surface, B cell-specific; autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

IT 674434-13-0P, Ghrelin (rat) 674434-15-2P, Ghrelin (mouse) 674434-17-4P, Ghrelin (human precursor) 674434-18-5P, Ghrelin (canis familiaris) 674434-20-9P, Ghrelin (swine) 674434-21-0P, Ghrelin (cattle) 674434-23-2P 674434-24-3P 674434-25-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

IT 541-59-3, Maleimide 1398-61-4, Chitin 7693-46-1, p-Nitrophenyl chloroformate 8063-16-9, Psyllium 9000-01-5, Gum arabic 9000-07-1, Carrageenan 9000-21-9, Furcellaran 9000-28-6, Gum ghatti 9000-30-0, Guar 9000-40-2, Locust bean gum 9000-65-1, Tragacanth 9000-69-5, Pectin 9002-84-0, Polytetrafluoroethylene 9002-89-5, Poly(vinyl alcohol) 9002-98-6, PEI 9003-01-4, Polyacrylic acid 9003-05-8, Polyacrylamide 9003-39-8, Poly(vinyl pyrrolidone)) 9004-34-6, Cellulose, biological studies 9004-54-0, Dextran, biological studies 9005-25-8, Starch, biological studies 9005-32-7D, Alginic acid, derivs. 9005-79-2, Glycogen, biological studies 9011-14-7, Poly(methyl methacrylate) 9012-36-6, Agarose 9012-72-0, Glucan 9012-76-4, Chitosan 9014-63-5, Xylan 9036-88-8, Mannan 9037-22-3, Amylopectin 9057-02-7, Pullulan 11078-30-1, Galactomannan 11138-66-2, Xanthan 12619-70-4D, Cyclodextrin, derivs. 24937-78-8, Poly(ethylene-co-vinyl acetate) 25087-26-7, Polymethacrylic acid 25249-16-5, Poly(2-hydroxyethyl methacrylate) 25322-68-3D, Polyethylene glycol, derivs. 26780-50-7D, Poly(lactide-co-glycolide), derivs. 37294-28-3, Xyloglucan 51751-43-0D, vinylene derivs. 54991-89-8, Tamarine 83869-56-1, GM-CSF 110865-71-9, Acetan
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

IT 674434-12-9P, DNA (rat ghrelin cDNA plus flanks) 674434-14-1P, DNA (mouse ghrelin cDNA plus flanks) 674434-16-3P, DNA (human ghrelin cDNA plus flanks) 674434-19-6P, DNA (swine ghrelin cDNA plus flanks) 674434-22-1P, DNA (cattle ghrelin cDNA plus flanks) 674434-26-5P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:144787 HCAPLUS Full-text
DOCUMENT NUMBER: 140:269420
TITLE: A Role for IL-10-Mediated HLA-DR7-Restricted T Cell-Dependent Events in Development of the Modified Th2 Response to Cat Allergen
AUTHOR(S): Reefer, Amanda J.; Carneiro, Raquel M.; Custis, Natalie J.; Platts-Mills, Thomas A. E.; Sung, Sun-Sang

J.; Hammer, Juergen; Woodfolk, Judith A.
CORPORATE SOURCE: Department of Internal Medicine, Asthma and Allergic Diseases Center, University of Virginia, Charlottesville, VA, 22908, USA
SOURCE: Journal of Immunology (2004), 172(5), 2763-2772
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 23 Feb 2004
AB Although high dose exposure to inhaled cat allergen (Fel d 1) can cause a form of tolerance (modified Th2 response), the T cell mechanism for this phenomenon has not been studied. T cell responses to Fel d 1 were characterized in both allergic (IgEpos) and modified Th2 (IgEnegIgGpos) responders as well as serum Ab-neg. controls (IgEnegIgGneg). Fel d 1 stimulated high levels of IL-10 in PBMC cultures from all individuals, with evidence of Th2 and Th1 cytokine skewing in allergic and control subjects, resp. Using overlapping peptides, epitopes at the N terminus of Fel d 1 chain 2 were shown to stimulate strong T cell proliferation and to preferentially induce IL-10 (peptide 2:1 (P2:1)) or IFN-γ (P2:2) regardless of the allergic status of the donor. Injection of cat extract during conventional immunotherapy stimulated expansion of IL-10- and IFN-γ-producing chain 2 epitope-specific T cells along with increased Fel d 1-specific serum IgG and IgG4 Ab. Six of 12 modified responders expressed the major HLA-DRB1 allele, *0701, and both P2:1 and P2:2 were predicted ligands for this allele. Cultures from DR7-pos. modified responders produced the highest levels of IL-10 to P2:1 in addition to other major and minor epitopes within chains 1 and 2. In the presence of anti-IL-10 mAb, both T cell proliferation and IFN-γ production were enhanced in a Fel d 1- and epitope-specific manner. We conclude that IL-10-producing T cells specific for chain 2 epitopes are relevant to tolerance induction, and that DR7-restricted recognition of these epitopes favors a modified Th2 response.
CC 15-9 (Immunochemistry)
ST interleukin Th1 Th2 cat allergen immunotherapy IgE IgG
IT Allergens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Fel d 1 (Felis domesticus, 1); IL-10-mediated, HLA-DR7-restricted T cell-dependent Th2 response to cat allergen)
IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA-DR, β-chain; IL-10-mediated, HLA-DR7-restricted T cell-dependent Th2 response to cat allergen)
IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA-DRB1; IL-10-mediated, HLA-DR7-restricted T cell -dependent Th2 response to cat allergen)
IT Immunotherapy
(IL-10-mediated, HLA-DR7-restricted T cell -dependent Th2 response to cat allergen)
IT Interleukin 10
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IL-10-mediated, HLA-DR7-restricted T cell -dependent Th2 response to cat allergen)
IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgE; IL-10-mediated, HLA-DR7-restricted T cell -dependent Th2 response to cat allergen)
IT Antibodies and Immunoglobulins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG4; IL-10-mediated, HLA-DR7-restricted T cell
-dependent Th2 response to cat allergen)
IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG; IL-10-mediated, HLA-DR7-restricted T cell
-dependent Th2 response to cat allergen)
IT T cell (lymphocyte)
(helper cell/inducer, TH1; IL-10-mediated, HLA-DR7-restricted T
cell-dependent Th2 response to cat allergen)
IT T cell (lymphocyte)
(helper cell/inducer, TH2; IL-10-mediated, HLA-DR7-restricted T
cell-dependent Th2 response to cat allergen)
IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ; IL-10-mediated, HLA-DR7-restricted T cell
-dependent Th2 response to cat allergen)
IT 672333-24-3 672333-25-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IL-10-mediated, HLA-DR7-restricted T cell
-dependent Th2 response to cat allergen)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:257008 HCAPLUS Full-text
DOCUMENT NUMBER: 138:285762
TITLE: Enhancement of bovine CD4(+) T cell-dependent immune responses induced by Anaplasma marginale Msp-1a DNA vaccine
AUTHOR(S): Mwangi, Waithaka
CORPORATE SOURCE: Washington State Univ., Pullman, WA, USA
SOURCE: (2002) 78 pp. Avail.: UMI, Order No. DA3058806
From: Diss. Abstr. Int., B 2003, 63(7), 3219
DOCUMENT TYPE: Dissertation
LANGUAGE: English
ED Entered STN: 03 Apr 2003
AB Unavailable
CC 15-2 (Immunochemistry)
ST cattle CD4 T cell Anaplasma Msp1a DNA vaccine
IT Anaplasma marginale
Bos taurus
Immunotherapy
Vaccines
(bovine CD4 T cell-dependent antigen-specific immune response enhancement induced by Anaplasma marginale Msp-1a DNA vaccine)
IT 83869-56-1, Granulocyte-macrophage colony-stimulating factor
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bovine CD4 T cell-dependent antigen-specific immune response enhancement induced by Anaplasma marginale Msp-1a DNA vaccine)

L69 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:617803 HCAPLUS Full-text
DOCUMENT NUMBER: 133:295207
TITLE: Constitutive PI3-K activity is essential for proliferation, but not survival, of Theileria parva-transformed B cells
AUTHOR(S): Baumgartner, Martin; Chaussepied, Marie; Moreau,

Marie-Francoise; Werling, Dirk; Davis, William C.; Garcia, Alphonse; Langsley, Gordon
CORPORATE SOURCE: Laboratoire de Signalisation Immunoparasitaire, Departement d'Immunologie, Institut Pasteur, Paris, 75724, Fr.
SOURCE: Cellular Microbiology (2000), 2(4), 329-339
CODEN: CEMIF5; ISSN: 1462-5814
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 Sep 2000
AB Theileria is an intracellular parasite that causes lymphoproliferative disorders in cattle, and infection of leukocytes induces a transformed phenotype similar to tumor cells, but the mechanisms by which the parasite induces this phenotype are not understood. Here, the authors show that infected B lymphocytes display constitutive phosphoinositide 3-kinase (PI3-K) activity, which appears to be necessary for proliferation, but not survival. Importantly, the authors demonstrate that one mechanism by which PI3-K mediates the proliferation of infected B lymphocytes is via the induction of a granulocyte-monocyte colony-stimulating factor (GM-CSF)-dependent autocrine loop. PI3-K induction of GM-CSF appears to be at the transcriptional level and, consistently, the authors demonstrate that PI3-K is also involved in the constitutive induction of AP-1 and NF-κB, which characterizes Theileria-infected leukocytes. The authors' results thus highlight a novel strategy exploited by the intracellular parasite Theileria to induce continued proliferation of its host leukocyte.
CC 15-8 (Immunochemistry)
ST phosphoinositide kinase Theileria B cell proliferation
IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(AP-1 (activator protein 1); phosphoinositide 3-kinase is involved in activation of AP-1 and NF-κB transcription factors of Theileria parva-transformed B cells)
IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-κB (nuclear factor κB); phosphoinositide 3-kinase is involved in activation of AP-1 and NF-κB transcription factors of Theileria parva-transformed B cells)
IT B cell (lymphocyte)
(infection; phosphoinositide 3-kinase is essential for proliferation, but not survival, of Theileria parva-transformed B cells and this involves granulocyte-macrophage colony-stimulating factor-dependent autocrine loop)
IT Cattle
Theileria parva
(phosphoinositide 3-kinase is essential for proliferation, but not survival, of Theileria parva-transformed B cells and this involves granulocyte-macrophage colony-stimulating factor-dependent autocrine loop)
IT Transcriptional regulation
(phosphoinositide 3-kinase is involved in activation of AP-1 and NF-κB transcription factors of Theileria parva-transformed B cells)
IT B cell (lymphocyte)
(proliferation; phosphoinositide 3-kinase is essential for

proliferation, but not survival, of Theileria parva-transformed B cells and this involves granulocyte-macrophage colony-stimulating factor-dependent autocrine loop)

IT 115926-52-8, Phosphoinositide 3-kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(phosphoinositide 3-kinase is essential for proliferation, but not survival, of Theileria parva-transformed B cells and this involves granulocyte-macrophage colony-stimulating factor-dependent autocrine loop)

IT 83869-56-1, GM-CSF
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(phosphoinositide 3-kinase is essential for proliferation, but not survival, of Theileria parva-transformed B cells and this involves granulocyte-macrophage colony-stimulating factor-dependent autocrine loop)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:590800 HCAPLUS Full-text
DOCUMENT NUMBER: 129:215709
TITLE: Malignant B cells expressing immunoglobulin-cytokine fusion proteins and use of the cells for immune therapy of B cell tumors
INVENTOR(S): Mocikat, Ralph
PATENT ASSIGNEE(S): GSF-Forschungszentrum fuer Umwelt und Gesundheit G.m.b.H., Germany
SOURCE: Ger., 10 pp.
CODEN: GWXXAW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 19716892 | C1 | 19980903 | DE 1997-19716892 | 19970422 <-- |
| EP 874054 | A2 | 19981028 | EP 1998-106176 | 19980403 <-- |
| EP 874054 | A3 | 20010411 | | |
| EP 874054 | B1 | 20030813 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| AT 247170 | T | 20030815 | AT 1998-106176 | 19980403 <-- |
| ES 2205303 | T3 | 20040501 | ES 1998-106176 | 19980403 <-- |
| JP 10295379 | A | 19981110 | JP 1998-126794 | 19980421 <-- |
| JP 3802677 | B2 | 20060726 | | |
| US 2002155111 | A1 | 20021024 | US 1998-64026 | 19980421 <-- |
| US 6673573 | B2 | 20040106 | | |
| US 2004072300 | A1 | 20040415 | US 2003-716580 | 20031118 <-- |
| PRIORITY APPLN. INFO.: | | | DE 1997-19716892 A | 19970422 <-- |
| | | | US 1998-64026 A3 | 19980421 <-- |

ED Entered STN: 17 Sep 1998
AB A vector for expression of Ig-cytokine fusion proteins in malignant B cells is disclosed. The vector comprises (a) a region of ≥1.5 kb which is homologous to an region of the μ- or κ-intron, (b) ≥1 DNA sequence which encodes an Ig domain or fragment thereof, (c) a cytokine-encoding DNA sequence, and (d) a

selectable marker, the expression of which is regulated by the cellular Cu or Cκ enhancer. The vector is site-specifically integrated into the B cell genome by homologous recombination. The recombinant B cells can be used for vaccination of patients with B cell cancers. A vector containing the 3'-fragment of the human IgG1 CH3 exon fused to mouse GM-CSF cDNA was integrated into mouse B lymphoma cell line MPC11. After radiation inactivation of these recombinant cells, they were used to vaccinate mice. These vaccinated mice lived longer upon challenge with wild-type tumor cells than did non-vaccinated mice.

IC ICM C12N015-79
ICS C12N015-85; C12N005-10; A61K048-00

CC 15-2 (Immunochemistry)
Section cross-reference(s): 3

ST Ig cytokine fusion B cell immunotherapy; tumor B cell immunotherapy

IT Antitumor agents
Antitumor agents
(B-cell leukemia; malignant B cells expressing Ig-cytokine fusion proteins and use of cells for immune therapy of B cell tumors)

IT Antitumor agents
Antitumor agents
(B-cell lymphoma; malignant B cells expressing Ig-cytokine fusion proteins and use of cells for immune therapy of B cell tumors)

IT Goat
Horse (Equus caballus)
Mouse
Rat
Sheep
(Ig DNA of; malignant B cells expressing Ig-cytokine fusion proteins and use of cells for immune therapy of B cell tumors)

IT Cytokines
Growth factors, animal
Interferons
Interleukin 12
Interleukin 13
Interleukin 2
Interleukin 4
Interleukin 7
Interleukins
Lymphokines
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fusion protein with Ig; malignant B cells expressing Ig-cytokine fusion proteins and use of cells for immune therapy of B cell tumors)

IT Immunoglobulins
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fusion protein with cytokine; malignant B cells expressing Ig-cytokine fusion proteins and use of cells for immune therapy of B cell tumors)

IT Antitumor agents

(multiple myeloma; malignant B cells expressing Ig-cytokine fusion proteins and use of cells for immune therapy of B cell tumors)

IT B cell (lymphocyte)
(recombinant; malignant B cells expressing Ig-cytokine fusion proteins and use of cells for immune therapy of B cell tumors)

IT Interferons
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(γ, fusion protein with Ig; malignant B cells expressing Ig-cytokine fusion proteins and use of cells for immune therapy of B cell tumors)

IT 83869-56-1P, GM-CSF
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fusion protein with Ig; malignant B cells expressing Ig-cytokine fusion proteins and use of cells for immune therapy of B cell tumors)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 9 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:132202 HCAPLUS Full-text
DOCUMENT NUMBER: 120:132202
TITLE: Reversal of feline leukemia virus infection by adoptive transfer of lectin/interleukin-2-activated lymphocytes, interferon-α, and zidovudine
AUTHOR(S): Zeidner, Nordin S.; Mathiason-DuBard, Candace K.; Hoover, Edward A.
CORPORATE SOURCE: Dep. Pathol., Colorado State Univ., Fort Collins, CO, USA
SOURCE: Journal of Immunotherapy with Emphasis on Tumor Immunology (1993), 14(1), 22-32
CODEN: JIEIEZ; ISSN: 1067-5582
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 19 Mar 1994

AB Previous exptl. studies utilizing human recombinant interferon-α-2b (IFNα-2b) alone or with zidovudine (AZT) to treat established feline leukemia virus (FeLV) infection resulted in a reduction in circulating virus throughout a 49-day treatment period. However, the anti-FeLV effect of IFNα was limited by the production of IFNα-neutralizing antibodies detected 7 wk after the start of treatment. AZT without IFNα had no effect on circulating virus load. To examine the hypothesis that combination chemoimmunotherapy might induce the clearance of FeLV infection, persistently infected cats were infused with activated lymphocytes, IFNα, and AZT 12 wk after infection with FeLV. Recipient cats received weekly infusions of 1.46+108 lymphocytes activated in vitro with lectin/IL-2 comprised of 98% T cells and an even distribution of CD4+ and CD8+ lymphocytes. FeLV infection was cleared in 4 of 9 cats receiving combined therapy after four adoptive cell transfers. These cats remained neg. for circulating virus during a 63-day treatment period (17 adoptive cell transfers) despite the production of anti-IFNα-neutralizing antibodies. Sequential development of virus neutralizing and virus envelope antibody titers were detected in those cats which cleared retroviremia, an antiviral response that was absent in untreated control animals or non-responders. Three of four responder cats remained neg. for FeLV 95 days after

treatment was discontinued. Treatment of cats with lymphocytes without chemotherapy failed to influence the course of FeLV infection. These results suggest that combined treatment using IFNα and adoptive lymphocyte transfer served to reconstitute antiviral humoral immunity, counteract immunosuppression, and induce the reversal of retroviremia.

CC 15-8 (Immunochemistry)
Section cross-reference(s): 1

ST feline leukemia virus interleukin 2 zidovudine; FAIDS adoptive immunotherapy interleukin 2 AZT

IT Immunosuppression
(feline leukemia virus-induced, in cats, interferon-α and adoptive T-cell immunotherapy and zidovudine reversal of)

IT Felis catus
(leukemia virus infection of, interferon-α and adoptive T-cell immunotherapy and zidovudine reversal of)

IT Lymphocyte
(T-cell, adoptive immunotherapy with, interferon-α and zidovudine and, feline leukemia virus infection in cats reversal by)

IT Acquired immune deficiency syndrome
(feline, leukemia virus-induced, in cats, adoptive T -cells and interferon-α and zidovudine combined chemoimmunotherapy reversal of)

IT Virus, animal
(feline leukemia, infection with, in cats, adoptive T -cells and interferon-α and zidovudine combined chemoimmunotherapy reversal of)

IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 2, Con A and, T-cells activated by, adoptive immunotherapy of cats with, interferon-α and zidovudine and, feline leukemia virus infection reversal by)

IT Antibodies
RL: BIOL (Biological study)
(neutralizing, to feline leukemia virus, interferon-α and adoptive T-cell immunotherapy and zidovudine induction of, in cats)

IT Interferons
RL: BIOL (Biological study)
(α-2b, zidovudine and adoptive T-cell immunotherapy and, feline leukemia virus infection in cats reversal by)

IT 30516-87-1, Zidovudine
RL: BIOL (Biological study)
(interferon-α and adoptive T-cell immunotherapy and, feline leukemia virus infection in cats reversal by)

IT 11028-71-0, Concanavalin A
RL: BIOL (Biological study)
(interleukin-2 and, T-cells activated by, adoptive immunotherapy of cats with, interferon-α and zidovudine and, feline leukemia virus infection reversal by)

L69 ANSWER 10 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:196565 HCAPLUS Full-text
DOCUMENT NUMBER: 112:196565

TITLE: Porcine polyclonal and monoclonal antibodies
INVENTOR(S): Osther, Kurt B.
PATENT ASSIGNEE(S): Bio-Research Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 9001066 | A1 | 19900208 | WO 1989-US3240 | | 19890726 <-- |
| W: JP | | | | | |
| RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | | |
| EP 429484 | A1 | 19910605 | EP 1989-908772 | | 19890726 <-- |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | | |
| JP 04500003 | T | 19920109 | JP 1989-508252 | | 19890726 <-- |
| PRIORITY APPLN. INFO.: | | | US 1988-224872 | A | 19880726 <-- |
| | | | WO 1989-US3240 | W | 19890726 <-- |

ED Entered STN: 26 May 1990

AB Methods for the preparation of porcine polyclonal, monoclonal, and anti-idiotypic antibodies to various antigens were developed. The methods follow procedures for the preparation of antibodies in other animals. These antibodies should have less side effects in humans treated with these antibodies. Swine antibodies should have potential in immunotherapy.

IC ICM C12P021-00
ICS C12N005-00; A61K039-395
CC 15-1 (Immunochemistry)
ST pig antigen monoclonal antibody immunotherapy
IT Swine
(anti-idiotypic and monoclonal and polyclonal antibodies from, preparation of, for immunotherapy in human)
IT Antigens
RL: PREP (Preparation)
(monoclonal and polyclonal antibodies to, preparation of, in pigs, immunotherapy in humans in relation to)
IT Antibodies
RL: PREP (Preparation)
(preparation of, in pigs, for immunotherapy in humans)
IT Hybridoma
(B-cell, monoclonal antibody-secreting, preparation of, from pigs, immunotherapy in humans in relation to)
IT Virus, animal
(cytomegalo-, anti-idiotypic and monoclonal antibodies to, preparation of, in pigs, immunotherapy in humans in relation to)
IT Antigens
RL: PREP (Preparation)
(hepatitis B surface, anti-idiotypic antibodies to, preparation of, in pigs, immunotherapy and internal image in relation to)
IT Antibodies
RL: PREP (Preparation)
(monoclonal, preparation of, in pigs, for immunotherapy in humans)
IT Lymphokines and Cytokines
RL: PREP (Preparation)
(tumor necrosis factor-α, monoclonal antibodies to, preparation of, in pigs, immunotherapy in humans in relation to)

=> d l69 11-19 iall abeq tech abex

L69 ANSWER 11 OF 32 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-371790 [35] WPIX
DOC. NO. CPI: C2003-098638 [35]
TITLE: Detecting a therapeutic antibody:antigen complex, useful for staging and monitoring hyperproliferative disease or autoimmune disease, comprises measuring circulating therapeutic antibody, antigen or antibody/antigen complex
DERWENT CLASS: B04; D16
INVENTOR: ALBITAR M; KEATING M J; MANSHOURI T
PATENT ASSIGNEE: (TEXA-C) UNIV TEXAS SYSTEM
COUNTRY COUNT: 99

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2003024993 | A2 | 20030327 | (200335)* | EN | 71 | [15] |
| US 20030068664 | A1 | 20030410 | (200335) | EN | | |
| EP 1438583 | A2 | 20040721 | (200447) | EN | | |
| AU 2002327037 | A1 | 20030401 | (200452) | EN | | |
| JP 2005533236 | W | 20051104 | (200574) | JA | 51 | |
| AU 2002327037 | A8 | 20051020 | (200615) | EN | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2003024993 | A2 | WO 2002-US30142 | 20020920 |
| US 20030068664 | A1 Provisional | US 2001-323679P | 20010920 |
| AU 2002327037 | A1 | AU 2002-327037 | 20020920 |
| EP 1438583 | A2 | EP 2002-761799 | 20020920 |
| US 20030068664 | A1 | US 2002-251144 | 20020920 |
| EP 1438583 | A2 | WO 2002-US30142 | 20020920 |
| JP 2005533236 | W | WO 2002-US30142 | 20020920 |
| JP 2005533236 | W | JP 2003-528839 | 20020920 |
| AU 2002327037 | A8 | AU 2002-327037 | 20020920 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| EP 1438583 | A2 | Based on | WO 2003024993 A |
| AU 2002327037 | A1 | Based on | WO 2003024993 A |
| JP 2005533236 | W | Based on | WO 2003024993 A |
| AU 2002327037 | A8 | Based on | WO 2003024993 A |

PRIORITY APPLN. INFO: US 2001-323679P 20010920
US 2002-251144 20020920
INT. PATENT CLASSIF.:
MAIN: G01N033-53
SECONDARY: G01N033-566
IPC ORIGINAL: A61K0039-395 [I,A]; A61K0039-395 [I,C]; G01N0033-564 [I,A]; G01N0033-564 [I,C]; G01N0033-574 [I,A]; G01N0033-574 [I,C]
IPC RECLASSIF.: A61K0039-395 [I,A]; A61K0039-395 [I,C]; A61P0013-00 [I,C]; A61P0013-08 [I,A]; A61P0013-10 [I,A]; A61P0019-00 [I,C]; A61P0019-02 [I,A]; A61P0025-00 [I,A]; A61P0025-00 [I,C]; A61P0027-00 [I,C]; A61P0027-02 [I,A]; A61P0035-00 [I,A]

; A61P0035-00 [I,C]; A61P0035-02 [I,A]; A61P0037-00 [I,C] ; A61P0037-02 [I,A]; A61P0037-06 [I,A]; A61P0005-00 [I,C] ; A61P0005-14 [I,A]; G01N0033-53 [I,A]; G01N0033-53 [I,C] ; G01N0033-543 [I,A]; G01N0033-543 [I,C]; G01N0033-564 [I,A]; G01N0033-564 [I,C]; G01N0033-574 [I,A]; G01N0033-574 [I,C]; G01N0033-577 [I,A]; G01N0033-577 [I,C]

BASIC ABSTRACT:

WO 2003024993 A2 UPAB: 20060202

NOVELTY - Detecting (M1) a therapeutic antibody:antigen complex comprising obtaining a sample from a patient who has undergone a course of immunotherapy with a therapeutic antibody that binds to a soluble circulating target antigen forming the complex, contacting the sample with a first monoclonal antibody, where the antibody captures the complex, contacting the complex with a labeled second antibody, and measuring the labeled complex, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) determining the efficacy of an antibody immunotherapy in a patient comprising detecting the levels of circulating antibody:antigen complexes;

(2) immunotherapy comprising administering to a patient a therapeutic antibody and detecting the presence of a circulating antibody:antigen complex;

(3) monitoring a therapeutic antibody therapy, a hyperproliferative disease, or an autoimmune disease, comprising measuring a therapeutic antibody:antigen complex in a patient sample or serum;

(4) determining tumor mass comprising obtaining a sample from a patient, contacting the sample with a first monoclonal antibody, where the antibody captures a soluble antigen in the sample, contacting the soluble antigen with a labeled second antibody, and measuring the labeled soluble antigen;

(5) staging a B cell, a T cell, and a myeloid hyperproliferative disease comprising determining or measuring the level of soluble CD20, CD52, and CD33, respectively, in a patient sample by a sandwich enzyme linked immunosorbent assay (ELISA);

(6) monitoring B cell hyperproliferative disease comprising measuring the level of soluble CD20, soluble anti-CD20 or CD20/anti-CD20 complexes in a patient sample by a sandwich ELISA;

(7) monitoring T cell or hematopoietic hyperproliferative disease comprising measuring the level of soluble CD52, soluble anti-CD52 or CD52/anti-CD52 complexes in a patient sample by a sandwich ELISA; and

(8) monitoring myeloid hyperproliferative disease comprising measuring the level of soluble CD33, soluble anti-CD33 or CD33/anti-CD33 complexes in a patient sample by a sandwich ELISA.

USE - Detecting or measuring the levels of therapeutic antibody:antigen complexes, soluble antigens or soluble therapeutic antibodies are useful for staging and monitoring B cell , T cell, hematopoietic or myeloid . hyperproliferative disease, e.g. chronic lymphocytic leukemia, acute lymphoblastic leukemia, myelodysplastic syndrome, chronic myelomonocytic leukemia, juvenile myelomonocyte leukemia, multiple myeloma, hairy cell leukemia, prolymphocytic leukemia, lymphoma, acute myelogenous leukemia, T -cell chronic lymphocytic leukemia or other T- cell diseases. The methods are also useful for monitoring a hyperproliferative disease such as cancer or neoplasm, e.g. melanoma, non-small cell lung cancer, small-cell lung cancer, lung hepatocarcinoma, retinoblastoma, astrocytoma, glioblastoma, gum, tongue, leukemia, neuroblastoma, head, neck, breast, pancreatic, prostate, renal, bone, testicular, ovarian, mesothelioma, cervical, gastrointestinal, lymphoma, brain, colon or bladder cancer, or an autoimmune disease, e.g. Sjogren's syndrome, rheumatoid arthritis, systemic lupus erythematosus, autoimmune thyroid disease, refractory ocular inflammatory disease, multiple sclerosis, or Wegener's granulomatosis (all claimed). M1 is also useful for determining a tumor mass. Measurement of soluble cell surface antigens and its complexes with therapeutic antibodies may also be used in designing more effective

therapeutic strategies. MANUAL CODE: CPI: B04-B04C; B04-B04D4; B04-G01; B04-G21; B11-C07A4;
B12-K04A; D05-A01A4; D05-A01B; D05-H09; D05-H11A

TECH BIOTECHNOLOGY - Preferred Method: The first monoclonal antibody or the therapeutic antibody used in any of the methods cited above is anti-CD20, anti-CD52 or anti-CD33, preferably rituximab, Campath-1H (RTM; alemtuzumab), or Mylotarg (RTM; gemtuzumab ozogamicin). The sample is serum or plasma, and the patient is a human patient. In detecting a therapeutic antibody:antigen complex, the first monoclonal antibody is bound to a solid surface. In determining the efficacy of an antibody immunotherapy in a patient, the step of detecting is by an enzyme linked immunosorbent assay (ELISA). The antibody immunotherapy is rituximab, Campath-1H (RTM; alemtuzumab), or Mylotarg (RTM; gemtuzumab ozogamicin). In the method of an immunotherapy, the antibody binds to a soluble antigen, which is shed from the cell surface. The antigen is CD20, CD52 or CD33. Detecting the presence of a circulating antibody:antigen complex is by ELISA. In monitoring an autoimmune disease, the therapeutic antibody is anti-CD52, preferably Campath-1H (RTM; alemtuzumab). The method further comprises measuring a second therapeutic antibody:antigen complex. The second therapeutic antibody is anti-CD20, preferably rituximab. The first and second antibody:antigen complexes are measured simultaneously or consecutively. In determining tumor mass, the sample used is plasma. The first monoclonal antibody is anti-CD20. The soluble antigen is CD20. Staging a B cell hyperproliferative disease further comprises determining the level of soluble CD52. Monitoring a B cell hyperproliferative disease further comprises measuring the level of soluble CD52, soluble anti-CD52 or CD52/anti-CD52 complexes. Monitoring a hematopoietic hyperproliferative disease further comprises measuring the amount of soluble CD20, soluble anti-CD20 or CD20/anti-CD20 complexes, or soluble CD33, soluble anti-CD33 and CD33/anti-CD33 complexes.

ABEX EXAMPLE - A 96-well polystyrene microplate was coated with capturing antibody for CD20 and washed. Plasma samples were added after 1:100 dilution in phosphate buffered saline and incubated. For detection, goat anti-human immunoglobulin that was horseradish peroxidase conjugated was used. The wells were then washed and 100 units of substrate were added for the development of color and incubated for 15-30 minutes with constant shaking. The reaction was then stopped with 15 mul of sodium chloride and the plates were read at 450 nm wavelength. Serial dilution of known number of molecules of synthetic CD20 peptide after binding at saturation to rituximab was used to generate a standard curve. Surface CD20 (sCD20)/rituximab immune complexes were detected in all 20 single samples from 20 chronic lymphocytic leukemia patients being treated with rituximab. sCD20/rituximab complexes increased with an increase in the levels of rituximab.

L69 ANSWER 12 OF 32 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-103456 [09] WPIX
DOC. NO. CPI: C2003-026147 [09]
TITLE: New fusion molecules comprising polypeptide sequences that bind to IgG inhibitory receptor and native IgE receptor, useful for treating IgE-mediated hypersensitivity reactions, e.g. asthma or allergies, or autoimmune diseases
DERWENT CLASS: B04; D16
INVENTOR: SAXON A; ZHANG K; ZHU D
PATENT ASSIGNEE: (SAXO-I) SAXON A; (REGC-C) UNIV CALIFORNIA; (ZHAN-I)

ZHANG K; (ZHUD-I) ZHU D

COUNTRY COUNT: 99

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC | |
|---|---|---|---|---|---|---|---|
| WO 2002088317 | A2 | 20021107 | (200309)* | EN | 116[11] | | <-- |
| US 20030064063 | A1 | 20030403 | (200325) | EN | | | |
| US 20030082190 | A1 | 20030501 | (200331) | EN | | | |
| AU 2002254753 | A1 | 20021111 | (200433) | EN | | | <-- |
| EP 1487480 | A2 | 20041222 | (200501) | EN | | | |
| ZA 2003008316 | A | 20050126 | (200513) | EN | 117 | | |
| JP 2005508138 | W | 20050331 | (200523) | JA | 193 | | |
| MX 2003010037 | A1 | 20040701 | (200545) | ES | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2002088317 | A2 | WO 2002-US13527 | 20020501 |
| US 20030064063 | A1 CIP of | US 2001-847208 | 20010501 |
| US 20030082190 | A1 | US 2001-847208 | 20010501 |
| US 20030064063 | A1 | US 2001-439 | 20011024 |
| AU 2002254753 | A1 | AU 2002-254753 | 20020501 |
| EP 1487480 | A2 | EP 2002-723997 | 20020501 |
| JP 2005508138 | W | JP 2002-585600 | 20020501 |
| EP 1487480 | A2 | WO 2002-US13527 | 20020501 |
| JP 2005508138 | W | WO 2002-US13527 | 20020501 |
| MX 2003010037 | A1 | WO 2002-US13527 | 20020501 |
| ZA 2003008316 | A | ZA 2003-8316 | 20031024 |
| MX 2003010037 | A1 | MX 2003-10037 | 20031031 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| AU 2002254753 | A1 | Based on | WO 2002088317 A |
| EP 1487480 | A2 | Based on | WO 2002088317 A |
| JP 2005508138 | W | Based on | WO 2002088317 A |
| MX 2003010037 | A1 | Based on | WO 2002088317 A |

PRIORITY APPLN. INFO: US 2001-439 20011024
US 2001-847208 20010501

INT. PATENT CLASSIF.:

MAIN: C12N-00; C12N015-09

IPC RECLASSIF.: A61K0035-66 [I,C]; A61K0035-76 [I,A]; A61K0038-00 [I,A]; A61K0038-00 [I,C]; A61K0048-00 [I,A]; A61K0048-00 [I,C]; A61P0011-00 [I,C]; A61P0011-02 [I,A]; A61P0011-06 [I,A]; A61P0017-00 [I,A]; A61P0017-00 [I,C]; A61P0017-04 [I,A]; A61P0019-00 [I,C]; A61P0019-02 [I,A]; A61P0025-00 [I,A]; A61P0025-00 [I,C]; A61P0029-00 [I,A]; A61P0029-00 [I,C]; A61P0003-00 [I,A]; A61P0003-00 [I,C]; A61P0037-00 [I,C]; A61P0037-08 [I,A]; A61P0043-00 [I,A]; A61P0043-00 [I,C]; C07K0016-00 [I,A]; C07K0016-00 [I,C]; C07K0016-18 [I,C]; C07K0016-28 [I,A]; C07K0019-00 [I,A]; C07K0019-00 [I,C]; C12N0001-15 [I,A]; C12N0001-15 [I,C]; C12N0001-19 [I,A]; C12N0001-19 [I,C]; C12N0001-21 [I,A]; C12N0001-21 [I,C]; C12N0015-09 [I,A]; C12N0015-09 [I,C]; C12N0005-10 [I,A]; C12N0005-10 [I,C]

BASIC ABSTRACT:

WO 2002088317 A2 UPAB: 20060118

NOVELTY - Isolated fusion molecule (I) comprising a first polypeptide sequence capable of specific binding to a native IgG inhibitory receptor consisting of an immune receptor tyrosine-based inhibitory motif (ITIM), expressed on mast cells, basophils or B cells, functionally connected to a second polypeptide sequence capable of specific binding directly or indirectly to a native IgE receptor (FcepsilonR), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a single-chain fusion molecule comprising the first polypeptide sequence capable of specific binding to a native human FcgammaRIIb receptor functionally connected to the second polypeptide sequence capable of specific binding directly or indirectly to native human FcepsilonRI receptor;

(2) a fusion molecule having, or which is at least 90% identical to a sequence of 569 amino acids, fully defined in the specification;

(3) an isolated nucleic acid molecule encoding any of the fusion molecules described above;

(4) a vector comprising and capable of expressing the nucleic acid molecule in (3);

(5) a host cell transformed with the vector in (4);

(6) a pharmaceutical composition comprising any of the fusion molecules in admixture with an ingredient;

(7) an article of manufacture comprising a container, the fusion molecule within the container, and a label or package insert on or associated with the container;

(8) a method for treating a condition associated with an IgE-mediated biological response, or autoimmune diseases;

(9) an isolated fusion molecule, as in (I), which is not capable of T cell interaction prior to internalization, where the first and second polypeptide sequences are other than antibody variable region sequences; and

(10) a method for preventing of, or symptoms resulting from, a type I hypersensitivity reaction in a subject receiving immunotherapy.

ACTIVITY - Antiasthmatic; Antiallergic; Antiinflammatory; Dermatological; Antiarthritic; Antirheumatic; Antidiabetic; Neuroprotective.

No biological data given.

MECHANISM OF ACTION - Immunotherapy; Gene therapy.

USE - The fusion molecules and compositions are useful for treating IgE-mediated biological response, preferably IgE-mediated hypersensitivity reaction, such as asthma, allergic rhinitis, atopic dermatitis, severe food allergies, chronic urticaria, angioedema or anaphylactic shock; or autoimmune diseases such as rheumatoid arthritis, type-I diabetes mellitus, or multiple sclerosis, and for preventing of, or symptoms resulting from, a type I hypersensitivity reaction in a subject receiving immunotherapy (claimed).

ADVANTAGE - The invention provides a safer and effective gamma-allergen bifunctional fusion molecules for allergy vaccination, as compared to conventional methods.

MANUAL CODE: CPI: B04-B04C; B04-C01; B04-E02H; B04-E08; B04-F0100E; B04-F1100E; B04-G01; B04-N02; B04-N0400E; B04-N06; B14-C03; B14-C09B; B14-G02A; B14-G02D; B14-K01A; B14-N04; B14-N17C; B14-S01; B14-S03; B14-S04; D05-H11; D05-H12B2; D05-H12E; D05-H14

TECH

BIOTECHNOLOGY - Preferred Fusion Molecule: The inhibitory receptor in (I) is a low-affinity IgG receptor FcgammaRIIb or FcepsilonRII (CD23), or a high affinity FcepsilonRI receptor. FcgammaRIIb and FcepsilonRI receptors are of human origin. The second polypeptide sequence is capable of specific binding to the native IgE receptor through a third polypeptide sequence. The second polypeptide sequence comprises an allergen sequence, specifically of a food or pollen allergen. The food allergen is selected

fro peanut, shellfish, mil, fish, soy, wheat, egg, or tree nut allergens. The first and second polypeptide sequences are connected through a linker, which is also a polypeptide sequence consisting of 5-25 amino acid residues, or are directly fused to each other. The first polypeptide comprises a sequence that is at least 90% identical to the hinge-CH2-CH3 portion of an IgG immunoglobulin heavy chain constant region that is encoded by a nucleic acid hybridizing under stringent conditions to the portion's coding sequence of 696 bp fully defined in the specification, or to a sequence of 232 amino acids, fully defined in the specification. The immunoglobulin can be IgG1, IgG2, IgG3, or IgG4. The immunoglobulin is preferably IgG1. The second polypeptide comprises a sequence that is at least 90% identical to the CH2-CH3-CH4 portion of an IgE immunoglobulin heavy chain constant region that is encoded by a nucleic acid hybridizing under stringent conditions to the complement of the portion's coding sequence of 1445 bp fully defined in the specification, to a sequence of 320 amino acids fully defined in the specification, to sequence of a native allergen, or any of the 167 sequences given in the specification. For the single-chain fusion molecule, the first polypeptide sequence comprises at least part of the CH2 and CH3 domains, and/or hinge of a native human IgG1 constant region. This sequence specifically comprises at least part of the hinge, CH2 and CH3 domains of a native human IgG1 heavy chain constant region, in the absence of a functionally CH1 region. The second polypeptide sequence comprises at least a part, or consists of the CH2, CH3 and CH4 domains of a native human IgE heavy chain constant region.

For the fusion molecule in (9), the second polypeptide sequence comprises an antigen sequence having at least a portion of an autoantigen sequence, or at least one autoantigenic epitope. The third polypeptide is an immunoglobulin specific for the autoantigen sequence, which is preferably an IgE class antibody. The autoantigen sequence is selected from rheumatoid arthritis, multiple sclerosis, and autoimmune type I diabetes mellitus autoantigens, or their portions. The autoantigen can be myelin basic protein (MBP), proteolipid protein, myelin oligodendrocyte glycoproteins, alphabeta-crystallin, myelin-associated glycoproteins, Po glycoproteins, PMP22, 2'3'-cyclic nucleotide 3'-phophohydrolase (CNPase), glutamic acid decarboxylase (GAD), insulin, 64 kD islet cell antigen (IA-2, also termed ICA512), phogrin (IA-2beta), type II collagen, human cartilage gp39 (HCgp39), or gp130-RAPS.

The autoantigen sequence present in this fusion molecule has at least 90% sequence identity with at least a portion of a native autoantigen sequence. The first polypeptide sequence comprises at least 85% sequence identity with a native IgG heavy chain constant region sequence of 330 amino acids, or to a sequence of 232 amino acids fully defined in the specification. The first polypeptide sequence is encoded by a nucleic acid hybridizing under stringent conditions to at least a portion of the complement of the IgG heavy chain constant region of 696 bp, fully defined in the specification. This fusion protein comprises at least one amino-terminal ubiquitination target motif, or proteasome proteolysis signal. The signal is selected from large hydrophobic amino acid residues, basic amino acid residues or acidic amino acid residues. The polypeptide linker further comprises the at least one proteasome proteolysis signal or endopeptidase recognition motifs. The endopeptidase recognition motif can be cysteine, aspartate or asparagine amino acid residues.

Preferred Article: The label or package insert comprises instructions for the treatment of IgE-mediated biological response, preferably IgE-mediated hypersensitivity reaction, such as asthma, allergic rhinitis, atopic dermatitis, severe food allergies, chronic urticaria, angioedema or anaphylactic shock, or for treatment or prevention of an immune disease.

PHARMACEUTICALS - Preferred Method: Treating a condition associated with

an IgE-mediated biological response comprises administering (I) in a subject, preferably human patient. The administration is preventing prior to the onset of the biological response. Treating an autoimmune disease in a subject comprises administering the fusion molecule in (9) to a subject diagnosed with or at risk of developing the autoimmune disease. Preventing of, or symptoms resulting from, a type I hypersensitivity reaction in a subject receiving immunotherapy comprises administering at least one fusion molecule in (9) to the subject. The second polypeptide comprises a sequence selected from at least a portion of an autoantigen, an allergen or at least a portion of an IgE immunoglobulin heavy chain constant region capable of binding to a native IgE receptor (FcepsilonR).

ABEX ADMINISTRATION - Dosage is 0.5-50 (preferably 1-10) mg/kg. Administration can be oral, intravenous, intra-arterial, intraperitoneal, subcutaneous, intranasal or intrapulmonary.

EXAMPLE - The expression vector containing chimeric Fcgamma-FcapproximatelyI gene was linearized in the PvuI site and transfected with into SP2/0 cells by electroporation. Stable transfectants were selected for growth in medium containing 1 mg/ml geneticin. Clones producing the fusion protein were identified by ELISA using plates coating anti-human IgE or IgG antibody. Supernatants from clones were added to wells, the bound protein was detected using goat anti-human IgE or IgG conjugated to alkaline phosphatases. The fusion protein was purified from the supernatants and ascites by using rProtein A column.

L69 ANSWER 13 OF 32 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-759837 [82] WPIX
DOC. NO. CPI: C2002-214753 [82]
TITLE: New Major Histocompatibility Complex (MHC) molecule construct, useful for treating, preventing, stabilizing or alleviating a disease involving MHC recognizing cells e.g., cancer
DERWENT CLASS: B04; D16
INVENTOR: AAMELLEM O; AMELLEM O; BUUS S; PETERSEN L O; RUUB E; RUUD E; SCHOELLER J; SCHOLLER J; WINTHER L
PATENT ASSIGNEE: (DAKO-N) DAKO AS; (DAKO-N) DAKOCYTOMATION DENMARK AS; (DYNA-N) DYNAL BIOTECH ASA
COUNTRY COUNT: 99

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC | |
|---|---|---|---|---|---|---|---|
| WO 2002072631 | A2 | 20020919 | (200282)* | EN | 304[57] | | <-- |
| NO 2003004020 | A | 20031106 | (200380) | NO | | | |
| EP 1377609 | A2 | 20040107 | (200404) | EN | | | |
| AU 2002240818 | A1 | 20020924 | (200433) | EN | | | <-- |
| JP 2005500257 | W | 20050106 | (200505) | JA | 439 | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2002072631 | A2 | WO 2002-DK169 | 20020313 |
| AU 2002240818 | A1 | AU 2002-240818 | 20020313 |
| EP 1377609 | A2 | EP 2002-706685 | 20020313 |
| JP 2005500257 | W | JP 2002-571544 | 20020313 |
| NO 2003004020 | A | WO 2002-DK169 | 20020313 |
| EP 1377609 | A2 | WO 2002-DK169 | 20020313 |
| JP 2005500257 | W | WO 2002-DK169 | 20020313 |

NO 2003004020 A NO 2003-4020 20030911

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| EP 1377609 A2 | Based on | WO 2002072631 A |
| AU 2002240818 A1 | Based on | WO 2002072631 A |
| JP 2005500257 W | Based on | WO 2002072631 A |

PRIORITY APPLN. INFO: US 2001-275470P 20010314
US 2001-275448P 20010314
US 2001-275447P 20010314
DK 2001-435 20010314
DK 2001-436 20010314
DK 2001-441 20010314

INT. PATENT CLASSIF.:

MAIN: C07K014-705; C07K017-02

SECONDARY: A61K038-17; C07K019-00; G01N033-566

IPC RECLASSIF.: A61K0038-00 [I,A]; A61K0038-00 [I,C]; A61K0045-00 [I,A]; A61K0045-00 [I,C]; A61K0047-48 [I,A]; A61K0047-48 [I,C]; A61P0001-00 [I,A]; A61P0001-00 [I,C]; A61P0001-04 [I,A]; A61P0001-16 [I,A]; A61P0011-00 [I,A]; A61P0011-00 [I,C]; A61P0011-06 [I,A]; A61P0013-00 [I,C]; A61P0013-08 [I,A]; A61P0013-10 [I,A]; A61P0013-12 [I,A]; A61P0015-00 [I,A]; A61P0015-00 [I,C]; A61P0017-00 [I,A]; A61P0017-00 [I,C]; A61P0017-06 [I,A]; A61P0019-00 [I,C]; A61P0019-02 [I,A]; A61P0025-00 [I,A]; A61P0025-00 [I,C]; A61P0029-00 [I,A]; A61P0029-00 [I,C]; A61P0003-00 [I,C]; A61P0003-10 [I,A]; A61P0031-00 [I,A]; A61P0031-00 [I,C]; A61P0031-12 [I,A]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0035-02 [I,A]; A61P0037-00 [I,C]; A61P0037-02 [I,A]; A61P0037-06 [I,A]; A61P0037-08 [I,A]; A61P0007-00 [I,A]; A61P0007-00 [I,C]; C07K0014-435 [I,C]; C07K0014-74 [I,A]; C07K0017-00 [I,C]; C07K0017-02 [I,A]; C12N0013-00 [I,A]; C12N0013-00 [I,C]; C12N0005-06 [I,A]; C12N0005-06 [I,C]; C12Q0001-00 [I,A]; C12Q0001-00 [I,C]; C12Q0001-04 [I,A]; C12Q0001-04 [I,C]; G01N0033-15 [I,A]; G01N0033-15 [I,C]; G01N0033-50 [I,A]; G01N0033-50 [I,C]; G01N0033-53 [I,A]; G01N0033-53 [I,C]; G01N0033-543 [I,A]; G01N0033-543 [I,C]; G01N0037-00 [I,A] ; G01N0037-00 [I,C]

BASIC ABSTRACT:

WO 2002072631 A2 UPAB: 20050903

NOVELTY - A new Major Histocompatibility Complex (MHC) molecule construct comprising a carrier molecule to which one or more MHC molecules are attached either directly or via one or more entities, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) detecting the presence or MHC recognizing cells in a sample;

(2) monitoring MHC recognizing cells;

(3) establishing a prognosis of a disease involving MHC recognizing cells;

(4) determining the status of, or the effectiveness of a medicament against, a disease involving MHC recognizing cells;

(5) diagnosing a disease involving MHC recognizing cells;

(6) a therapeutic composition comprising as active ingredient a MHC molecule construct;

(7) up-regulating, down-regulating or modulating an immune response in an animal, including a human being;

(8) treating an animal, including a human being;

(9) inducing energy of a cell in animal, including a human being;
(10) an adoptive cellular immunotherapeutic method;
(11) obtaining MHC recognizing cells; or
(12) producing a therapeutic composition.

ACTIVITY - Cytostatic; Antiinflammatory; Dermatological; Antiasthmatic; Antidiabetic; Anti-HIV; Virucide; Antiarteriosclerotic; Antiulcer; Antirheumatic; Antiarthritic; Antipsoriatic; Immunosuppressive. No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - The MHC molecule construct is useful as a therapeutic composition in in vivo or ex vivo therapy, for treating, preventing, stabilizing or alleviating a disease involving MHC recognizing cells, for monitoring MHC recognizing cells or establishing a prognosis of a disease or diagnosing a disease, or determining the status of a disease or the effectiveness of a medicament against a disease, involving MHC recognizing cells, e.g., chronic inflammatory bowel disease such as Crohn's disease or ulcerative colitis, sclerosis, type I diabetes, rheumatoid arthritis, psoriasis, atopic dermatitis, asthma, malignant melanoma, renal carcinoma, breast cancer, lung cancer, cancer of the uterus, cervical cancer, prostate cancer, brain cancer, head and neck cancer, leukemia, cutaneous lymphoma, hepatic carcinoma, colorectal cancer, bladder cancer, rejection-related disease, Graft-versus-host- related disease, or a viral disease associated with hepatitis, Acquired Immunodeficiency Syndrome (AIDS), measles, pox, chicken pox, rubella or herpes. The MHC molecule construct is also useful for flow cytometric, histological or cytological method (all claimed.) MANUAL CODE: CPI: B02-C01; B02-R; B03-G; B04-B01B; B04-B03C;
B04-B04C7; B04-C01; B04-C02; B04-C03; B04-E01; B04-F01; B04-G01; B04-H01; B04-H05; B04-K01; B04-L01; B04-N04; B06-H; B07-H; B11-C07B3; B11-C08E; B12-K04A; B12-K04B; B14-A02; B14-C09B; B14-E10C; B14-G02C; B14-H01; B14-K01; B14-N12; B14-N17; B14-S03; B14-S04; D05-H09; D05-H10; D05-H11; D05-H17C

TECH

BIOTECHNOLOGY - Preferred Construct: The MHC molecule construct is in soluble form in a solubilizing medium. It is immobilized directly onto a biodegradable solid or semi-solid support via a linker, a spacer, or antibody or antibody derivative or its fragment, prior to expansion. The expansion is carried out in the presence of one or more MHC molecule constructs, optionally one or more biologically active molecules and optionally feeder cells such as dendritic cells or feeder cells. The support is selected from glass or chamber slides, dishes or petridishes microtiter plates having one or more wells, particles, beads, biodegradable particles, sheets, gels, filters, membranes (e. g. nylon or polymer membranes), fibers, capillaries, needles, microtiter strips, tubes, plates or wells, combs, pipette tips, micro arrays or chips. Preferably, the support is selected from beads and particles, which are polymeric beads, polymeric particles, magnetic beads, magnetic particles, supermagnetic beads or particles. The MHC molecule construct comprises peptide free or filled MHC molecules. The total number of MHC molecules of the construct is from 1 - 25, 1 - 50 or 1 - 100. The peptides to fill the peptide free MHC molecules, and the MHC molecule construct comprising peptide free molecules are provided separately. The MHC molecule construct further comprises one or more biologically active molecules selected from proteins, co-stimulatory molecules, cell modulating molecules, receptors, accessory molecules, adhesion molecules, natural ligands, toxic molecules, antibodies, recombinant binding molecules or their combinations. The biologically active molecules also comprises:
(1) proteins such as MHC Class I-like proteins like MIC A, MIC B, CD1d, human leukocyte antigen (HLA) E, HLA F, HLA G, HLA H, ULBP-1, ULBP-2, and ULBP-3;
(2) co-stimulatory molecules such as CD2, CD3, CD4, CD5, CD8, CD9, CD27,

CD28, CD30, CD69, CD134 (OX40), CD137 (4-1BB), CD147, CDw150 (SLAM), CD152 (CTLA-4), CD153 (CD30L), CD40L (CD154), NKG2D, ICOS, HVEM, HLA Class II, PD-1, Fas (CD95), FasL expressed on T and/or NK cells, CD40, CD48, CD58, CD70, CD72, B7.1 (CD80), B7.2 (CD86), B7RP-1, B7H3, PD-L1, PD-L2, CD134L, CD137L, ICOSL, LIGHT expressed on APC and/or tumor cells;
(3) cell modulating molecules such as CD16, NKp30, NKp44, NKp46, NKp80, 2B4, KIR, LIR, CD94/NKG2A, CD94/NKG2C expressed on natural killer (NK) cells, interferon (IFN)-alpha, IFN-beta, IFN-gamma, interleukin (IL)-1, IL-2, IL-3, IL-4, IL-6, IL-7, IL-8, IL-10, IL-11, IL-12, IL-15, CSFs (colony-stimulating factors), vitamin D3, IL-2 toxins, cyclosporin, FK-506, rapamycin, transforming growth factor (TGF)-beta, clotrimazole, nitrendipine, and charybdotoxin, accessory molecules such as lymphocyte function associated molecule (LFA)-1, CD11a/18, CD54 (intercellular adhesion molecule (ICAM)-1) CD106 (VCAM), and CD49a,b,c,d,e,f/CD29 (VLA-4);
(4) adhesion molecules such as ICAM-1, ICAM-2, GlyCAM-1, CD34, anti-LFA-1, anti-CD44, anti-beta7, chemokines, CXCR4, CCR5, anti-selectin L, anti-selectin E, and anti-selectin P;
(5) toxic molecules such as cyclophosphamide, methrotrexate, Azathioprine, mizoribine, 15-deoxuspergualin, neomycin, staurosporine, genestein, herbimycin A, Pseudomonas exotoxin A, saporin, Rituxan, Ricin, gemtuzumab ozogamicin, Shiga toxin, heavy metals like inorganic and organic mercurials, and FN18-CRM9, radioisotopes such as incorporated isotopes of iodide, cobalt, selenium, tritium, and phosphor, and haptens such as DNP, and digoxiginin; or
(6) antibodies or antibody derivatives or fragments, or combinations of (1) - (5).
The MHC molecule construct further comprises one or more labeling compounds that are attached to the carrier molecule, one or more of the binding entities or one or more of the MHC molecules. The labeling compound, which is directly or indirectly detectable, is a fluorescent label, an enzyme label, a radioisotope, a chemiluminescent label, a bioluminescent label, a polymer, a metal particle, a hapten, an antibody or a dye. It is selected from:
(1) fluorescent labels such as 5-(and 6)-carboxyfluorescein, 5- or 6-carboxyfluorescein, 6-(fluorescein)-5-(and 6)-carboxamido hexanoic acid, fluorescein isothiocyanate (F)TC), rhodamine, tetramethylrhodamine, and dyes such as Cy2, Cy3 and Cy5, optionally substituted coumarin including AMCA, PerCP, phycobiliproteins including R-phycoerythrin (RPE) and allophycoerythrin (APC), Texas Red, Princeston Red, Green fluorescent protein (GFP) and their analogs, and conjugates of R-phycoerythrin or allophycoerythrin and e.g. Cy5 or Texas Red, and inorganic fluorescent labels based on semiconductor nanocrystals (like quantum dot and Qdot (RTM) nanocrystals), and time-resolved fluorescent labels based on lanthanides like Eu3+ and Sm3+;
(2) haptens such as DNP, biotin, and digoxiginin;
(3) enzymatic labels such as horse radish peroxidase (HRP), alkaline phosphatase (AP), betagalactosidase (GAL), glucose-6-phosphate dehydrogenase, beta-N-acetylglucosaminidase, beta-glucuronidase, invertase, Xanthine Oxidase, firefly luciferase and glucose oxidase (GO);
(4) luminescence labels such as luminol, isoluminol, acridinium esters, 1,2-dioxetanes and pyridopyridazines; or
(5) radioactivity labels such as incorporated isotopes of iodide, cobalt, selenium, tritium, and phosphor.
The carrier molecule, which is soluble molecule, consists of:
(1) polysaccharides including dextrans, carboxy methyl dextran, dextran polyaldehyde, carboxymethyl dextran lactone, and cyclodextrins, pullulans, schizophyllan, scleroglucan, xanthan, gellan, O-ethylamino guaran, chitins and chitosans including 6-0- carboxymethyl chitin and N-carboxymethyl chitosan;

(2) derivatized cellolosics including carboxymethyl cellulose, carboxymethyl hydroxyethyl cellulose, hydroxy-ethyl cellulose, 6-amino-6-deoxy cellulose and O-ethyl-amine cellulose;
(3) hydroxylated starch, hydroxypropyl starch, hydroxyethyl starch, carrageenans, alginates, and agarose, synthetic polysaccharides including ficoll and carboxy-methylated ficoll;
(4) vinyl polymers including poly(acrylic acid), poly(acrylamides), poly(acrylic esters), poly(2-hydroxy ethyl meth-acrylate), poly(methyl methacrylate), poly(maleic acid), poly(maleic anhydride), poly(acrylamide), poly(ethyl-co-vinyl acetate), poly(methacrylic acid), poly(vinyl-alcohol), poly(vinyl alcohol-co-vinyl chloroacetate), aminated poly(vinyl alcohol), and their co block polymers;
(5) poly ethylene glycol (PEG) or polypropylene glycol or poly(ethylene oxide-co-propylene oxides) containing polymer backbones including linear, comb-shaped or StarBurst (RTM) dendrimers;
(6) poly amino acids including polylysines, polyglutamic acid, polyurethanes, poly(ethylene imines), pluriol;
(7) proteins including albumins, immunoglobulins, and virus-like proteins (VLP); or
(8) polynucleotides, DNA, PNA, LNA, oligonucleotides or oligonucleotide dendrimer constructs.
The MHC molecule is a vertebrate MHC molecule such as a human, murine, rat, porcine, bovine or avian molecule. Preferably the MHC molecule is a human MHC molecule. It is a peptide free MHC molecule. The MHC molecule comprises:
(1) a MHC Class I molecule consisting of a heavy chain, a heavy chain combined with a beta2m, a heavy chain combined with a peptide or a heavy chain/beta2m dimer with a peptide;
(2) a MHC Class II molecule consisting of an alpha/beta dimer, an alpha/beta dimer with a peptide, alpha/beta dimer combined through an affinity tag and an alpha/beta dimer combined through an affinity tag with a peptide; or
(3) a MHC Class I like molecule or MHC Class II like molecule.
Two of the MHC molecules or the peptides harbored by the MHC molecules are either the same or different. The MHC molecules are attached to the carrier molecule directly or via one or more binding entities. 1 - 2, 1 - 3, 1 - 4, 1 - 6, 1 - 8 or 1 - 10 MHC molecules are attached to the carrier molecule by each binding entity. The binding entity is selected from streptavidin (SA) and avidin or their derivatives, biotin, immunoglobulins, antibodies (monoclonal, polyclonal, and recombinant), antibody fragments and their derivatives, leucine zipper domain of AP-1 (jun and fos), hexa-his (metal chelate moiety), hexa-hat GST (glutathione S-tranferase) glutathione affinity, Calmodulin-binding peptide (CBP), Strep-tag, Cellulose Binding Domain, Maltose Binding Protein, S-Peptide Tag, Chitin Binding Tag, Immunoreactive Epitopes, Epitope Tags, E2Tag, HA Epitope Tag, Myc Epitope, FLAG Epitope, AU1 and AU5 Epitopes, Glu-Glu Epitope, KT3 Epitope, IRS Epitope, Btag Epitope, Protein Kinase-C Epitope, VSV Epitope, lectins that mediate binding to a diversity of compounds, including carbohydrates, lipids and proteins, e.g. Con A (Canavalia ensiformis) or WGA (wheat germ agglutinin) and tetranectin or Protein A or G (antibody affinity).
Preferred Composition: The adjuvant of the composition is selected from saponins such as Quil A and Qs-21, oil in water emulsions such as MF59, MPL, PLG, PLGA, aluminium salts, calcium phosphate, water in oil emulsions such as IFA (Freund's incomplete adjuvant) and CFA (Freund's complete adjuvant), interleukins such as IL-1beta IL-2, IL-7, IL-12, and INFgamma, Adju-Phos (RTM), glucan, antigen formulation, biodegradable microparticles, Cholera Holotoxin, liposomes, DDE, DMEA, DMPC, DMPG, DOC/Alum Complex, ISCOMsr, muramyl dipeptide, monophosphoryl lipid A, muramyl tripeptide, and phospatidylethanolamine, preferably from saponins

such as Quil A and Qs-21, MF59, MPL, PLG, PLGA, calcium phosphate, and aluminium salts. The excipient is selected from diluents, buffers, suspending agents, wetting agents, solubilizing agents, pH-adjusting agents, dispersing agents, preserving agents, and/or colorants.
Preferred Method: Detecting the presence of MHC recognizing cells in a sample comprises:
(a) providing a sample suspected of comprising MHC recognizing cells;
(b) contacting the sample with a MHC molecule construct; and
(c) determining any binding of the MEC molecule construct, the binding of which indicates the presence of MHC recognizing cells.
Monitoring MHC recognizing cells or establishing a prognosis of a disease or diagnosing a disease, or determining the status of a disease, involving MHC recognizing cells comprises:
(a) providing a sample suspected of comprising MHC recognizing cells;
(b) contacting the sample with a MHC molecule construct; and
(c) determining any binding of the MHC molecule construct.
Determining the effectiveness of a medicament against a disease involving MHC recognizing cells comprises:
(a) providing a sample from a subject receiving treatment with a medicament;
(b) contacting the sample with a MHC molecule construct;
(c) determining any binding of the MHC molecule construct.
The determination of the binding is carried out by inspection in a microscope, by light, by fluorescence, by electron transmission or by flow cytometry. The MHC recognizing cells are selected from subpopulations of CD3+ T-cells, gamma, delta T-cells
, alpha, beta T-cells, CD4+ T-cells
, T helper cells, CD8+ Tcells, Suppressor T-cells,
CD8+ cytotoxic T-cells, cytotoxic T-
cells (CTL)s, natural killer (NK) cells, NKT cells, LAK cells, and MAK. The MHC recognizing cells are involved in a disease of inflammatory, auto-immune, allergic, viral, cancerous, infectious, allo- or xenogene (graft versus host and host versus graft) origin. Obtaining MHC recognizing cells comprises:
(a) bringing a sample from a subject comprising MHC recognizing cells into contact with a MHC molecule construct, where the MHC recognizing cells become bound to the MHC molecule construct;
(b) isolating the bound MHC molecule construct and the MHC recognizing cells; and
(c) expanding the MHC recognizing cells to a clinically relevant number.
The isolation is carried out by applying a magnetic field or by flow cytometry. The MHC recognizing cells are liberated from the MHC molecule construct prior to expansion. The disease consists of chronic inflammatory bowel disease such as Crohn's disease or ulcerative colitis, sclerosis, type I diabetes, rheumatoid arthritis, psoriasis, atopic dermatitis, asthma, malignant melanoma, renal carcinoma, breast cancer, lung cancer, cancer of the uterus, cervical cancer, prostate cancer, brain cancer, head and neck cancer, leukemia, cutaneous lymphoma, hepatic carcinoma, colorectal cancer, bladder cancer, rejection-related disease, Graft-versus-host-related disease, or a viral disease associated with hepatitis, acquired immunodeficiency syndrome (AIDS), measles, pox, chicken pox, rubella or herpes. The sample is selected from histological material, cytological material, primary tumors, secondary organ metastasis, fine needle aspirates, spleen tissue, bone marrow specimens, cell smears, exfoliative cytological specimens, touch preparations, oral swabs, laryngeal swabs, vaginal swabs, bronchial lavage, gastric lavage, from the umbilical cord, and from body fluids such as blood (e.g. from a peripheral blood mononuclear cell (PBMC) population isolated from blood or from other blood-derived preparations such as leukopheresis products), from sputum samples, expectorates, and bronchial aspirates. The sample is

mounted on a support. An adoptive cellular immunotherapeutic method, inducing energy of a cell, or up-regulating, down-regulating or modulating an immune response in, or treating an animal, including a human being comprises administering the therapeutic composition. Producing a therapeutic composition comprises:
(a) providing the MHC molecule construct solubilizing or dispersing the MHC molecule construct in a medium suitable for therapeutic substances; and
(b) optionally adding other adjuvants and/or excipients.
The method also comprises:
(a) obtaining MHC recognizing cells using the MHC molecule construct;
(b) expanding such MHC recognizing cells to a clinically relevant number,
(c) formulating the obtained cells in a medium suitable for administration; and
(d) optionally adding adjuvants and/or excipients.

ABEX ADMINISTRATION - Administered via oral, rectal, nasal, topical or parenteral route, e.g., intravenous, intramuscular, intraarticular, subcutaneous, intradermal, epicutaneous/transdermal, and intraperitoneal, or by infusion (claimed). No specific dosage is given.
EXAMPLE - The preparations of SA conjugated dextrans of different molecular sizes were mixed with amounts of human leukocyte antigen (HLA) complexes corresponding to a ratio of two biotinylated HLA Class I molecules per SA molecule. The HLA molecule was added directly to a solution of SA-conjugated dextrans. Thus, MHC molecule constructs were formed.

L69 ANSWER 14 OF 32 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-314696 [35] WPIX
CROSS REFERENCE: 1990-193272; 1993-336582; 1995-036097; 1995-036466; 1996-040230; 2002-712476; 2003-531074; 2003-801206; 2004-061648; 2005-464777; 2006-099382; 2006-342137; 2006-688311
DOC. NO. CPI: C2002-091436 [35]
TITLE: Inducing T cell population to proliferate, useful in cancer therapy, comprises activating T cells by contacting T cells in vitro with immobilized anti-CD3 antibody and stimulating accessory molecule on T cell surface
DERWENT CLASS: B04; D16
INVENTOR: GRAY G S; JUNE C H; NABEL G J; RENNERT P D; THOMPSON C B
PATENT ASSIGNEE: (GEMY-C) GENETICS INST INC; (UNMI-C) UNIV MICHIGAN
COUNTRY COUNT: 1

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC | |
|---|---|---|---|---|---|---|---|
| US 6352694 | B1 | 20020305 | (200235)* | EN | 71[31] | | <-- |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| US 6352694 B1 | CIP of | US 1994-253964 | 19940603 |
| US 6352694 B1 | | US 1995-403253 | 19950310 |

PRIORITY APPLN. INFO: US 1995-403253 19950310
US 1994-253964 19940603
INT. PATENT CLASSIF.:

IPC RECLASSIF.: C07K0014-435 [I,C]; C07K0014-705 [I,A]; C07K0016-18 [I,C] ; C07K0016-28 [I,A]; C12N0005-06 [I,A]; C12N0005-06 [I,C] ; C12N0005-08 [I,A]; C12N0005-08 [I,C]

BASIC ABSTRACT:

US 6352694 B1 UPAB: 20060119

NOVELTY - Inducing T cell population to proliferate for use in therapy comprising activating T cells by contacting T cells in vitro with anti-CD3 antibody (Ab1) which is immobilized on solid phase surface (I) and stimulating accessory molecule on T cell surface in vitro with:

(a) anti-CD28 antibody (Ab2); or

(b) stimulatory form of natural ligand for CD28 (NLC) such as B7-1 or B7-2, where NLC or Ab2 is also immobilized on (I), is new.

ACTIVITY - Cytostatic; antimicrobial; anti-HIV.

MECHANISM OF ACTION - Ex vivo T cell therapy. Peripheral blood mononuclear cells (PBMC) were obtained from a normal blood donor, and either the purified CD4+ T (10 to the power of 5 cells/well) cells or whole PBMC (10 to the power of 5 cells/well) were activated with phytohaemagglutinin (PHA) (5 microgram/ml) or with anti-CD3 and anti-CD28 coated beads (3 beads per T cell ). The cells were infected with a T cell trophic variant of human immunodeficiency virus (HIV)-1 (US1) or a monocyte trophic variant (BAL) on day 2 of culture. The level of virus expression was quantitated in the culture supernatants on day 7 by the Spearmen-Karber method. In PBMC, high levels of virus were expressed if the cells were stimulated with PHA whereas very low or no levels of virus were detected in cultures stimulated with anti-CD3 and anti-CD28 antibodies. This result was obtained whether or not plastic adherent monocytes/macrophages (M/M) were added to the culture (10 to the power of 4 cells per well). Thus, stimulation of CD+ T cells infected with HIV with anti-CD3 and anti-CD28 resulted in much lower amounts of HIV particles produced as compared to the conventional method of T cell stimulation with PHA and interleukin (IL)-2.

USE - For inducing a population of T cells to proliferate in sufficient numbers for use in therapy e.g., for treating cancer or an infectious disease (claimed). The method can be used to selectively expand the population of CD28+, CD4+, CD8+, CD28RA+ or CD28RO+ T cells for immunotherapy. The T cell population resulting by the method can be genetically transduced and used for immunotherapy or can be used for in vitro analysis of infectious agents such as human immunodeficiency virus (HIV). Proliferation of a population of CD4+ T cells obtained from an individual infected with HIV can be achieved and the cells rendered resistant to HIV infection. Following the expansion of the T cells to sufficient numbers, the expanded T cells are restored to the individual. Also CD4+ T cells expanded by the above mentioned is useful for treating HIV infection in an individual. When CD4+ T cells from an HIV infected individual are stimulated with Ab1 and Ab2 antibodies attached to solid phase support the cell culture proliferates exponentially and the amount of HIV particles produced is significantly reduced as compared to conventional methods for stimulating T cells. Also a population of tumor-infiltrating lymphocytes can be obtained from an individual afflicted with cancer and the T cells stimulated to proliferate to sufficient numbers and restored to the individual. The supernatants from cultures of T cells expanded from above mentioned method are useful as a rich source of cytokines and can be used to sustain T cells in vivo or ex vivo. Stimulating and expanding a population of antigen specific T cells are useful in therapeutic conditions where it is desirable to upregulate an immune response.

ADVANTAGE - The method enables the selective stimulation of the T cell population to proliferate and expand to significant numbers in vitro in the absence of exogenous growth factors or accessory cells. T cell proliferation is induced without the need for an antigen, thus providing an expanded T cell population which is polyclonal with respect to antigen reactivity. The method provides for sustained proliferation of a selected population of CD4+ or CD8+ T cells over an extended period of time to yield a multi-fold increase in the number of these cells relative

to the original T cell population. Preferably, the method allows for expansion of population of T cells in numbers sufficient to reconstitute an individual's total CD4+ or CD8+ T cell population. The CD4+ T cells from an HIV infected individual are expanded ex vivo with Ab1 and Ab2 on solid phase surface, the presence of anti-retroviral agents may not be required in the culture to limit replication HIV. Since anti-retroviral drugs have toxic effects on cells, no retroviral agents or reduced amounts of these agents will result in expansion to higher T cell numbers.

MANUAL CODE: CPI: B04-F04; B04-G01; B04-G21; B04-N06; B06-F03; B14-A02B1; B14-H01; D05-H08; D05-H11A

TECH BIOTECHNOLOGY - Preferred Method: Ab1 is a anti-human CD3 monoclonal antibody and Ab2 is an anti-human CD28 monoclonal antibody. Ab1 and Ab2 are immobilized on (I) via a covalent modification e.g., via an avidin-biotin complex, or are directly immobilized on (I). Both Ab1 and Ab2 are whole antibodies. (I) is a bead preferably a magnetic immunobead, or is a tissue culture dish. The T cells are induced to proliferate for at least three days and preferably for seven days. The T cells are preferably induced to proliferate to about 100 fold (more preferably 100000 fold) the original T cell population.

ABEX WIDER DISCLOSURE - The following are disclosed: - (1) compositions comprising an agent that provides a co-stimulatory signal to a T cell for T cell expansion e.g., Ab2, B7-1 or B7-2 ligand coupled to a solid phase surface which may additionally include an agent that provides a primary activation signal to the T cell e.g., Ab1 coupled to the same solid phase surface; - (2) compositions comprising each agent coupled to different solid phase surfaces (i.e., an agent that provides a primary T cell activation signal coupled to a first solid phase surface and an agent that provides a co-stimulatory signal coupled to a second solid phase surface); - (3) kits comprising the above mentioned compositions; - (4) selectively expanding a specific subpopulation of T cells from a mixed population of T cells e.g., specifically enriching a population of CD28+ T cells in CD4+ T cells; and - (5) selectively expanding a population of either TH1 or TH2 cells or from a population of CD4+ T cells.

EXAMPLE - Peripheral blood CD28+ T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies. CD4+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody (mAb) and removing the CD8+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28+, CD4+ T cells were cultured in defined medium. At an initial density of 2.0 x 10 to the power of 6/ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse immunoglobulin G (IgG) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either human interleukin (hIL)-2 or anti-CD28 monoclonal antibody (mAb) (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5 x 10 to the power of 6/ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells were removed and placed at 1.0 x 10 to the power of 6/ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb. The culture vessel initially contained 50 x 10 to the power of 6 cells, and the cells were cultured in an optimal amount of mitogenic lectin phytohaemagglutinin (PHA), or cultured with cyclic stimulation of plastic immobilized anti-CD3 mAb in the presence of interleukin 2 or anti-CD28 mAb 9.3. The cells cultured in PHA alone did not proliferate, with all cells dying by about day 20 of culture. In contrast, the cells grown in anti-CD3 with IL-2 or anti-CD28 entered a logarithmic growth phase, with equal rates of growth for the

first three weeks of culture. However, the anti-CD3 cultures began to diverge in growth rates during the fourth week of culture, with the IL-2 fed cells entering a plateau phase after a 2.8 log 10 expansion. In contrast, the cultures grown in the presence of anti-CD28 remained in logarithmic growth until the sixth week of culture, at which time there had been a 3.8 log 10 expansion. Thus, CD28 receptor stimulation, perhaps by anti-CD28 crosslinking, was able to stimulate the growth of CD4+ T cells in the absence of fetal calf serum or accessory cells, and furthermore, about 10-fold more cells can be obtained using anti-CD28 antibody consistently yielded more CD4+ T cells than expansion using IL-2 (e.g., up to 1000-fold more cells).

L69 ANSWER 15 OF 32 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-123319 [13] WPIX
DOC. NO. CPI: C2001-035888 [13]
TITLE: Immunogenic compositions comprising Flt-3 ligand encoding polynucleotide and one or more antigen, or cytokine encoding polynucleotides, useful for suppressing tumor growth and for treating autoimmune diseases (e.g. rheumatoid arthritis)
DERWENT CLASS: B04; D16
INVENTOR: HERMANSON G G
PATENT ASSIGNEE: (VICA-N) VICAL INC
COUNTRY COUNT: 21

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC | |
|---|---|---|---|---|---|---|---|
| WO 2001009303 | A2 | 20010208 | (200113)* | EN | 149[9] | | <-- |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2001009303 A2 | | WO 2000-US20679 | 20000731 |

PRIORITY APPLN. INFO: US 1999-146170P 19990730
INT. PATENT CLASSIF.:
IPC RECLASSIF.: A61K0039-39 [I,A]; A61K0039-39 [I,C]; C07K0014-435 [I,C]; C07K0014-475 [I,A]

BASIC ABSTRACT:

. WO 2001009303 A2 UPAB: 20050524

NOVELTY - Immunogenic compositions comprising Flt-3 ligand encoding polynucleotide and one or more antigen or cytokine encoding polynucleotides, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are provided for:

(1) a composition (C1) comprising:

(a) 1 ng to 10 mg of a nucleic acid comprising a first polynucleotide (N1) which hybridizes, at 42 degrees Centigrade in 50% formamide, 5 x SSC (saline sodium chloride), 50 mM sodium phosphate, 5 x Denhardt's solution, 10% dextran sulfate, and 20 microg/ml denatured, sheared salmon sperm DNA, followed by washing at 65 degrees Centigrade in 0. 1 x SSC and 0. 1 % sodium dodecyl sulfate (SDS) (w/v), to a reference nucleic acid having a 839, 852, 1152, 663, 519, 1080, 537, or 859 (S1-S8, respectively) nucleotide sequence defined in the specification, or their complements, where the first polynucleotide encodes a polypeptide having immunity-enhancing activity when administered to a vertebrate;

(b) 1 ng to 30 mg of a nucleic acid (N2) comprising a second polynucleotide encoding one or more antigens, or one or more cytokines, where

the first and second polynucleotides are non-infectious and non-integrating, and are operably associated with control sequences which direct their expression;

(2) a composition (C2) comprising:

(a) 1 ng to 10 mg of a nucleic acid comprising a first polynucleotide (N3) which encodes a first polypeptide which, except for at least one but not more than 20 amino acid substitutions, deletions, or insertions, is identical to a second polypeptide selected from amino acids 28 to 163 of the 231 amino acid sequence (S9), amino acids 27 to 160 of 235 amino acid sequence (S15), or amino acids 27 to 185 of 235 amino acid sequence (S17) (all sequences are defined in the specification), where the first polypeptide has immunity-enhancing activity when administered to a vertebrate;

(b) 1 ng to 30 mg of N2, where the first and second polynucleotides are non-infectious and non-integrating, and are operably associated with control sequences which direct their expression;

(3) a pharmaceutical composition (C3) comprising:

(a) 1 ng to 10 mg of a nucleic acid molecule comprising a first polynucleotide (N4) encoding an amino acid sequence that is at least 90%, preferably 97%, identical to a reference amino acid sequence selected from S9, 189 (S10), 220 (S11), 232 (S12), 172 (S14), S15, 178 (S16), S17 or 185 (S18) amino acid sequence defined in the specification, where % identity is determined using the Bestfit program with default parameters, and the polypeptide has immunity-enhancing activity when administered to a vertebrate;

(b) 1 ng to 30 mg of N2, where the first and second polynucleotides are non-infectious and non-integrating, and are operably associated with control sequences which direct their expression;

(4) a method (M1) for enhancing an immune response in a vertebrate, comprising administering C1, C2 or C3 to a tissue of the vertebrate, where the first and second polynucleotides are expressed in vivo in an amount effective for a polypeptide expressed by the first polynucleotide to enhance the immunogenicity of one or more antigens, or one or more cytokines; and

(5) a method (M2) of suppressing tumor growth in a mammal, comprising administering C1, C2 or C3 to a tissue of a mammal.

ACTIVITY - Antirheumatic; antiarthritic; immunostimulant; antiviral; antibacterial; antifungal; antiparasitic; cytostatic; immunosuppressive; protozoacide; antiinflammatory.

Three groups of mice were used in the study. One group (n=9) was co-injected with VR6200 (a Flt-3 ligand-encoding plasmid) and VR1623 (bicistronic chimeric Id vector) (100 microg each) on days 0, 14, and 28, and challenged with 500 38C13 tumor cells two weeks following the last injection. Control groups (n=10 each) were co-injected with VR1623 and VR1051 (control plasmid), or VR1605 (generic cloning vector comprising the constant regions of human kappa light chain and gamma 1 heavy chain separated by a CITE (cap independent translational enhancer)) or alone (200 microg) on days 0, 14, and 28, and challenged with 500 38C13 tumor cells two weeks following the last injection.

The co-injection of a Flt-3 ligand-encoding plasmid (100 microg of VR6200) with a tumor-specific antigen-encoding plasmid (100 microg of VR1623) significantly enhanced protection from tumor challenge. Eight out of nine mice injected with VR1623 and VR6200 survived the challenge as compared to zero out of ten mice surviving after being immunized with VR1623 and the control plasmid, VR1051. This increased survival was statistically significant p=0.00007. Furthermore, the co-injection of a Flt-3 ligand-encoding plasmid (VR6200) with an idiotype antigen-encoding plasmid (VR1623) resulted in greatly enhanced anti-Id antibody titer relative to mice injected with VR1623 and VR1051, or with VR1623 alone.

MECHANISM OF ACTION - Vaccine.

USE - The compositions are useful for suppressing tumor growth in a mammal. The tumor is melanoma, glioma or lymphoma, particularly B-cell lymphoma. The compositions are used in conjunction with additional cancer treatments (claimed).

The immunogenic compositions can also be used for the prophylactic and/or therapeutic treatment of:

(a) bacterial (e.g. Bacillus infections), viral (e.g. hepatitis B and C in humans), parasitic (e.g. malaria) and fungal infections;

(b) autoimmune diseases (e.g. rheumatoid arthritis and osteoarthritis);

(c) cancer (e.g. cancers of stomach, small intestine, liver, etc.); and

(d) Aujeszky's disease in pigs.

Various other examples of these diseases are given in the specification.

MANUAL CODE: CPI: B04-E02F; B04-E03B; B04-E03F; B14-A01; B14-A02; B14-A03; B14-A04; B14-C09A; B14-C09B; B14-G01; B14-G02D; B14-H01; B14-S11; B14-S12; D05-H07; D05-H12A; D05-H12B2

TECH

PHARMACEUTICALS - Preferred Composition: N1 encodes a polypeptide comprising 15, preferably 150, contiguous amino acids of the S9, S10, S11, S12, 220 (S13), S14, S15, S16, S17 or S18. All amino acid sequences are defined in the specification. Preferably, N1 encodes:

(a) residues 28-163, 1-163, 28-189 or 1-189 of S9;

(b) residues 28-231 of S8 and 28-232 of S12;

(c) residues 1-231 of S8 and 1-232 of S12;

(d) residues 28-220, or 1-220 of S11;

(e) residues 28-172 or 1-172 of S14;

(f) residues 27-160, 1-160, 1-185, 27-235, 1-235 or 27-185 of S15;

(g) residues 27-178 or 1-178 of S16; or

(h) residues 1-185, 27-185, 27-235 or 1-235 of S17.

Alternatively, N1 encodes 3 amino acid regions comprising amino acid residues 34-41, 107-113 and 142-150 of S15 arranged consecutively.

Alternatively, N1 encodes a polypeptide selected from:

(a) a polypeptide which, except for at least one amino acid substitution at an amino acid position selected from residues 34, 110, 144, or 147 of S15, is identical to amino acids 27 to 160 of S15; and

(b) a polypeptide which, except for at least one amino acid substitution at an amino acid position selected from residues 34, 110, 144 or 147 of S17, is identical to amino acids 27 to 185 of S17;

The amino acid substitution increases the immunity enhancing activity of the polypeptide.

In C2, the second polypeptide comprises:

(a) residues 1-163, 28-189 or 1-189 of S9;

(b) residues 28-231 of S8 and 28-232 of S12;

(c) residues 1-231 of S8 and 1-232 of S12;

(d) residues 28-220, or 1-220 of S11;

(e) residues 28-172 or 1-172 of S14;

(f) residues 1-160, 1-185, 27-235, 1-235 or 27-185 of S15;

(g) residues 27-178 or 1-178 of S16; or

(h) residues 1-185, 27-235 or 1-235 of S17.

The number of amino acid substitutions, deletions, or insertions is not more than 10, preferably 1. The amino acid substitutions, deletions or insertions do not occur in regions identical to amino acids 34 to 41, 107 to 113, and 142 to 150 of S15.

N3 encodes a polypeptide selected from:

(a) a polypeptide having amino acids 27 to 160 of S15, where at least one amino acid substitution occurs at an amino acid position selected from residues 34, 110, 144 or 147; or

(b) a polypeptide having amino acids 27 to 185 of S17, where at least one amino acid substitution occurs at an amino acid position selected from residues 34, 110, 144 or 147.

The amino acid substitution increases the immunity enhancing activity of the polypeptide.

In all compositions, the nucleic acid molecule of (a) is selected from VR6200 (5322 nucleotide sequence defined in the specification) or VR6230

(5310 nucleotide sequence defined in the specification).
In all the compositions, the antigen is a viral antigen, a bacterial antigen, a protozoan parasite antigen, a helminth parasite antigen, a fungal antigen, an ectoparasite antigen, a tumor associated antigen, or a self antigen associated with autoimmunity. The tumor-associated antigen comprises a tumor-specific immunoglobulin variable region, a GM2 antigen, a Tn antigen, an sTn antigen, a Thompson-Friedenreich antigen (TF), a Globo H antigen, a Le(y) antigen, a MUC (undefined)-1 antigen, a MUC2 antigen, a MUC3 antigen, a MUC4 antigen, a MUC5AC antigen, a MUC5B antigen, a MUC7 antigen, a carcinoembryonic antigen, a beta chain of human chorionic gonadotropin (hCG beta) antigen, a HER2/neu antigen, a PSMA (undefined) antigen, a EGFRvII (epidermal growth factor receptor vIII) antigen, a KSA (undefined) antigen, a prostate specific antigen (PSA), a PSCA (undefined) antigen, a GP (glycoprotein) 100 antigen, a MAGE-1 (undefined) antigen, a MAGE-2 antigen, a TRP 1 (undefined) antigen, a TRP 2 antigen, or a tyrosinase antigen.
The tumor-associated antigen comprises a B-cell lymphoma-specific idiotype determinant. The tumor specific antigen further comprises an immunoglobulin constant region. The second polynucleotide encoding the tumor-associated antigen is polycistronic, i.e. it comprises: (a) a first cistron encoding a protein comprising a light chain variable region of a B-cell lymphoma immunoglobulin having a tumor-specific idiotype determinant, fused to a constant region; and (b) a second cistron encoding a protein comprising a heavy chain variable region of a B-cell lymphoma immunoglobulin having a tumor-specific idiotype determinant, fused to a constant region.
The constant region is derived from a heterologous species relative to the variable region. The two cistrons are organized in a transcription unit under the control of a single promoter and the second polynucleotide further comprises an internal ribosome entry site positioned between the cistrons. The second polynucleotide is selected from VR1623 (7521 nucleotide sequence defined in the specification) and VR1642 (7528 nucleotide sequence defined in the specification). The first and second polynucleotides are present in a single nucleic acid molecule which encodes a fusion protein comprising a Flt-3 ligand and one or more antigens, or one or more cytokines.
The compositions further comprise a cationic lipid. The cationic lipid comprises a compound selected from DMRIE ((+/-)-N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-1-propanium bromide), GAP-DMORIE ((+/-)-N-(3-aminopropyl)-N,N-dimethyl-2,3-bis(syn-9-tetradeceneyloxyl)-1-propanaminium bromide) (preferred) or GAP-DLRIE ((+/-)-N-(3-aminopropyl)-N,N-dimethyl-2,3-(bis-dodecylozy)-1-propanaminium bromide). The cationic lipid further comprises one or more co-lipids such as DOPE (undefined), DPyPE (undefined) (preferred) or DMPE (3,4-Dimethoxy-phenylethylamine). The cationic lipid:co-lipid molar ratio ranges from 2:1 to 1:2.
The control sequences are selected from a promoter, an enhancer, an operator, a repressor or a transcription termination signal. Preferably, the control sequence is a promoter selected from cytomegalovirus promoter, a simian virus 40 promoter or a retrovirus promoter. The first and second polynucleotides are DNA or RNA. The first and second polynucleotides comprise one or more regions regulating cell specific or tissue specific gene expression. The region is tumor cell or tumor tissue specific.
The compositions further comprise 1 ng to 10 mg of a nucleic acid molecule comprising a third polynucleotide encoding a cytokine, or its active fragment, where the third polynucleotide is non-infectious and non-integrating, and is operably associated with control sequences which direct its expression. The cytokine is selected from Granulocyte macrophage colony stimulating factor (GM-CSF), Granulocyte colony stimulating factor (G-CSF), Macrophage colony stimulating factor (M-CSF), colony stimulating factor (CSF), erythropoietin, interleukin (IL)-2, IL-3,

IL-4, IL-5, IL-6, IL-7, IL-8, IL- 10, IL- 12, IL- 15, IL-18, interferon (IFN)-alpha, IFN-beta, IFN-gamma, IFN-omega, IFN-tau, IFN-gamma inducing factor I, tumor growth factor-beta, RANTES (Regulated upon activation normal T-cell expressed and secreted), Macrophage inflammation protein (MIP)-1-alpha, MIP-1-beta, Leishmania elongation initiating factor (LEIF), stromal cell derived factor 1 (SDF-1), and MCP-3 (undefined).

Preferred Method: in M1, the tissue is selected from muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus rectum, nervous system, eye, gland, tongue or connective tissue. The vertebrate is a mammal, preferably a human. The construct is free from association with transfection-facilitating proteins, viral particles, liposomes, cationic lipids, and calcium phosphate precipitating agents.

In M2, the tumor is selected from melanoma, glioma, or lymphoma. The method further comprises one or more additional cancer treatment methods selected from surgery, radiation therapy, chemotherapy, immunotherapy or gene therapy. The composition is administered prior to the commencement of the one or more additional cancer treatment methods. Alternatively, the composition is administered during the practice of the one or more additional cancer treatment methods. Alternatively, the composition is administered at the end of one or more additional cancer treatment methods.

ABEX WIDER DISCLOSURE - Also disclosed as new are kits comprising the immunogenic compositions.

ADMINISTRATION - The first and second polynucleotides are administered onto a mucosal surface (e.g. skeletal muscle, smooth muscle, or myocardium), intravenously, intramuscularly by injection, transdermally, interdermally, subcutaneously, orally, intraocularly, vaginally, rectally, or by inhalation. Administration may also be mediated by a catheter. The administration is mediated by a device selected from a particle accelerator, a pump, an intradermal applicator, a biolistic injector, a pneumatic injector, a sponge depot, a pill or a tablet. When treating B-cell lymphoma, the composition is administered intramuscularly (all claimed). No dosage data given.

SPECIFIC MICROORGANISMS - The viral antigen is derived from adenoviruses, alphaviruses, apthoviruses, caliciviruses, coronaviruses, coxsackieviruses, distemper viruses, Ebola viruses, enteroviruses, flaviviruses, hepatitis viruses, herpesviruses, immunodeficiency viruses, infectious peritonitis viruses, influenza viruses, leukemia viruses, Marburg viruses, oncogenic viruses, orthomyxoviruses, papilloma viruses, parainfluenza viruses, paramyxoviruses, parvoviruses, pestiviruses, picoma viruses, pox viruses, rabies viruses, reoviruses, respiratory syncytial viruses, retroviruses, rhinoviruses, rotaviruses, cancer-causing viruses or cancer-related viruses. - The bacterial antigen is derived from an organism having a genus selected from Actinomyces, Bacillus, Bacteroides, Bordetella, Bartonella, Borrelia, Brucella, Campylobacter, Capnocytophaga, Chlamydia, Clostridium, Corynebacterium, Coxiella, Dermatophilus, Enterococcus, Ehrlichia, Escherichia, Francisella, Fusobacterium, Haemobartonella, Haemophilus, Helicobacter, Klebsiella, L-form bacteria, Leptospira, Listeria, Mycobacteria, Mycoplasma, Neisseria, Neorickettsia, Nocardia, Pasteurella, Peptococcus, Peptostreplococcus, Pneumococcus, Proteus, Pseudomonas, Rickettsia, Rochalimaea, Salmonella, Shigella, Staphylococcus, Streplococcus, Treponema or Yersinia. - The protozoan parasite antigen is derived from an organism having a genus selected from Babesia, Balantidium, Besnoitia, Cryptosporidium, Eimeria, Encephalitozoon, Entamoeba, Giardia, Hammondia, Hepatozoon, Isospora, Leishmania, Microsporidia, Neospora, Nosema, Pentatrichomonas, Plasmodium, Pneumocystis, Sarcocystis, Schistosoma, Theileria, Toxoplasma, or

Trypanosoma. - The helminth parasite antigen is derived from an organism having a genus selected from Acanthocheilonema, Aelurostrongylus, Ancylostoma, Angiostrongylus, Ascaris, Brugia, Bunostomum, Capillaria, Chabertia, Cooperia, Crenosoma, Dictyovaulus, Dioctophyme, Dipetalonema, Diphyllobothrium, Diplydium, Dirofilaria, Dracunculus, Enterobius, Filaroides, Haemonchus, Lagochilascaris, Loa, Mansonella, Muellerius, Nanophyetus, Necator, Nematodirus, Oesophagostomum, Onchocerca, Opisthorchis, Oslertagia, Paraftlaria, Paragonimus, Parascaris, Physaloptera, Protostrongylus, Setaria, Spirocerca, Spirometra, Stephanqfilaria, Strongyloides, Strongylus, Thelazia, Toxascaris, Toxocara, Trichinella, Trichostrongylus, Trichuris, Uncinaria, or Wuchereria. - The fungal antigen is derived from an organism having a genus selected from Absidia, Acremonium, Alternaria, Aspergillus, Basidiobolus, Bipolaris, Blastomyces, Candida, Coccidioides, Conidiobolus, Cryptococcus, Curvalaria, Epidermophyton, Exophiala, Geotrichum, Histoplasma, Madurella, Malassezia, Microsporum, Moniliella, Mortierella, Mucor, Paecilomyces, Penicillium, Phialemonium, Phialophora, Prototheca, Pseudallescheria, Pseudomicrodochium, Pythium, Rhinosporidium, Rhizopus, Scolecobasidium, Sporothrix, Slemphylium, Trichophylon, Trichosporon or Xylohypha. - The ectoparasite antigen is derived from an organism selected from fleas, ticks, mosquitos, sand flies, black flies, horse flies, horn flies, deer flies, tsetse flies, stable flies, myiasis-causing flies, biting gnats, ants, spiders, lice, mites, bed bugs or kissing bugs.

EXAMPLE - VR6200 expresses a secreted form of murine Flt-3 ligand. Total bone marrow RNA was isolated from a single C57B1/6 mouse using a Qiagen Rneasy Mini Kit. Approximately 150 microg of total RNA was obtained. - First strand cDNA was synthesized from 5 microg of the bone marrow total RNA using the SuperScript Preamplification System (Life Technologies). Two microl of bone marrow cDNA was used in a 50 microl polymerase chain reaction (PCR) using native Pfu polymerase from Stratagene with the supplied buffer. The forward PCR primer CACGAATTCGCCGCCACCATGACAGTGCTGGCGC CA and the reverse primer GCCGCTAGCTCACTGCCTGGGCCGAGGCTCT were synthesized by Sigma-Genosys. The forward primer codes for an EcoRI restriction site followed by a consensus Kozak sequence followed by the Flt-3 ligand ATG start site and coding region. The reverse primer codes for an NheI restriction site, and places a stop codon just 5' of the transmembrane region. The final cDNA construct contains nucleotides 32 through 598 of the Flt-3 ligand cDNA (GenBank accession 4 L23636, a 829 nucleotide sequence defined in the specification). The construct codes for a secreted form of murine Flt-3 ligand lacking the transmembrane and cytoplasmic domains, and having the 189 amino acid sequence defined in the specification. This form of murine Flt-3 ligand has been shown to be biologically active. - The PCR cycling conditions were 94 degrees Centigradefor 5 minutes followed by 30 cycles of: 94 degrees Centigrade for 30 seconds, 55 degrees Centigrade for 30 seconds, and 72 degrees Centigrade for 1 minute. The PCR product was digested with EcoRI and NheI and cloned into the same sites of the plasmid VR-1051 (Norman et al., Vaccine, June 1997, 15(8):801-3) using standard molecular biology techniques. Individual clones were then sequenced and a perfect clone was named VR6200 (5322 nucleotide sequence defined in the specification).

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|---|---|---|
| L69 | ANSWER 16 OF 32 | WPIX COPYRIGHT 2007 THE THOMSON CORP on STN |
| ACCESSION NUMBER: | | 2000-679548 [66] WPIX |
| DOC. NO. CPI: | | C2000-206692 [66] |
| TITLE: | | Enhancing antigen-presentation capabilities of T -cells for cancer immunotherapy, by contacting cells with an immunostimulatory oligonucleotide |
| DERWENT CLASS: | | B04; D16 |
| INVENTOR: | | MARTIN-OROZCO E; RAZ E |

PATENT ASSIGNEE: (REGC-C) UNIV CALIFORNIA
COUNTRY COUNT: 21

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC | |
|---|---|---|---|---|---|---|---|
| WO 2000062787 | A1 | 20001026 | (200066)* | EN | 42[8] | | <-- |
| AU 2000046426 | A | 20001102 | (200107) | EN | | | <-- |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2000062787 | A1 | WO 2000-US9664 | 20000411 |
| AU 2000046426 | A | AU 2000-46426 | 20000411 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| AU 2000046426 | A | Based on | WO 2000062787 A |

PRIORITY APPLN. INFO: US 1999-292278 19990415
INT. PATENT CLASSIF.:
IPC RECLASSIF.: A61K0039-00 [I,A]; A61K0039-00 [I,C]; A61K0039-39 [I,A]; A61K0039-39 [I,C]; C12N0005-06 [I,A]; C12N0005-06 [I,C]

BASIC ABSTRACT:

WO 2000062787 A1 UPAB: 20060117

NOVELTY - Inducing activation of T-cells to respond to an antigen, comprising contacting antigen-presenting cells (APC) with an immunostimulatory oligonucleotide (ISS-ODN) to produce APCs with enhanced antigen presenting capabilities compared to antigen-activated APCs, is new. APCs with enhanced antigen-presentation capabilities present the antigen to T-cells.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) producing APCs with enhanced antigen presentation capabilities compared to antigen activated APCs, by contacting APC with ISS-ODN;

(2) APCs produced by the method of (1); and

(3) a composition comprising the APCs of (2).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Activator of APC; vaccine. No biological data is given.

USE - The method is useful for cancer immunotherapy. ISS-ODN is used to enhance tumor antigen presenting capacity of tumor cells, and is useful for treating tumors. Tumor cells treated with ISS-ODN ex vivo are useful as vaccines.

ADVANTAGE - ISS-ODN treated APCs are induced to take up antigen through upregulation of Fc-receptor expression, present antigen through upregulation of major histocompatibility complex (MHC) Class I and II, as well as CD1d expression, produce co-stimulatory factors (B7 and CD40), provide cell-to-cell adhesion through upregulation of intercellular adhesion molecule (ICAM) expression, and increase Th1 stimulatory cytokine production, all at levels greater than that achieved through contact of APC with antigen alone. MANUAL CODE: CPI: B04-E01; B04-F04; B14-G01; B14-H01; B14-H01B; B14-S11C; D05-H07

TECH

BIOTECHNOLOGY - Preferred Cells: APCs are B cells, bone-marrow derived macrophages or tumor cells. The antigen presented to T-cells, is a tumor antigen. T-cells

are activated through in vitro or in vivo contact with APCs which have enhanced antigen presentation capabilities.

ABEX ADMINISTRATION - ISS-ODN is administered through intranasal, subcutaneous, ophthalmic, systemic or other parenteral routes in a dosage of 1-50 micro-g/ml.

EXAMPLE - Splenic T cells and Antigen presenting cells (APC) were prepared from BALB/c TCR-OVA transgenic (TG) mice. The animals were injected with immunostimulatory oligonucleotide (ISS-ODN) on days 0 and 7. On day 14 mice were sacrificed and the spleens were harvested. To enrich APCs, splenocytes were treated with anti-CD8 antibodies and anti-CD4 antibodies followed by incubation with guinea pig complement and fixed with MMC (undefined). Splenocytes were obtained from naive TCR-OVA TG mice and purified for T cells by negative selection. The resultant T-cell preparations were mixed with the same number of accessory cells and hen egg ovalbumin for 3-4 days. The cultures were incubated with (3H)-thymidine and harvested. Incubation of murine splenocytes with ISS-ODN for 48 hours resulted in the up-regulation of a distinctive profile of cell-surface markers on the B220+ population. Incubation with ISS clearly enhanced the expression of major histocompatibility complex ( MHC) class I, class II, B7-2, CD40, intercellular adhesion molecule (ICAM), CD16/32, interferon (IFN)-gammaR (receptor), and IL-2R. In contrast, CD23 expression was down-regulated, while no differences in the expression of CD49b, CD1d, CD49a, CD49c-f, interleukin (IL)-1R and IL-6R were observed in the ISS-ODN treated cells. The cell surface profile induced by ISS stimulation of purified B splenocytes was similar to that observed for B cells (B220+) from ISS stimulated splenocytes.

L69 ANSWER 17 OF 32 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-316905 [27] WPIX
CROSS REFERENCE: 1991-164136; 1992-331670; 1993-152472; 1993-152473; 1993-320744; 1994-126807; 1995-373765; 1998-567590; 1999-590385; 2000-146862; 2000-181812; 2000-601477; 2001-549074
DOC. NO. CPI: C2000-095772 [27]
TITLE: New human T cell reactive feline protein useful for reducing or abolishing individual's allergic response to cat allergen comprising two different covalently linked peptide chains
DERWENT CLASS: B04; C06; D16
INVENTOR: BRAUER A W; GARMAN R D; GEFTER M L; GREENSTEIN J L; GRIFFITH I J; KUO M; MORGENSTERN J P; ROGERS B L
PATENT ASSIGNEE: (IMMU-N) IMMULOGIC PHARM CORP
COUNTRY COUNT: 1

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC | |
|---|---|---|---|---|---|---|---|
| US 6048962 | A | 20000411 | (200027)* | EN | 104[37] | | <-- |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| US 6048962 | A CIP of | US 1989-431565 | 19891103 |
| US 6048962 | A CIP of | US 1991-662276 | 19910228 |
| US 6048962 | A CIP of | US 1991-807529 | 19911213 |
| US 6048962 | A CIP of | US 1992-857311 | 19920325 |
| US 6048962 | A CIP of | US 1992-884718 | 19920515 |
| US 6048962 | A CIP of | US 1993-6116 | 19930115 |

US 6048962 A Div Ex US 1994-300928 19940902
US 6048962 A US 1995-430014 19950427

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| US 6048962 A | CIP of | US 5547669 A |

PRIORITY APPLN. INFO: US 1995-430014 19950427
US 1989-431565 19891103
US 1991-662276 19910228
US 1991-807529 19911213
US 1992-857311 19920325
US 1992-884718 19920515
US 1993-6116 19930115
US 1994-300928 19940902

INT. PATENT CLASSIF.:
IPC RECLASSIF.: A61K0038-00 [N,A]; A61K0038-00 [N,C]; A61P0037-00 [I,C]; A61P0037-08 [I,A]; C07K0014-415 [I,A]; C07K0014-415 [I,C]; C07K0014-435 [I,C]; C07K0014-47 [I,A]; C07K0014-725 [I,A]; C07K0016-18 [I,A]; C07K0016-18 [I,C]; C12N0015-62 [I,A]; C12N0015-62 [I,C]; G01N0033-50 [I,A]; G01N0033-50 [I,C]

BASIC ABSTRACT:

US 6048962 A UPAB: 20050410

NOVELTY - An isolated naturally occurring cat protein allergen (I), human T cell reactive feline protein (TRFP), comprising two different covalently linked peptide chains with a molecular weight of 20 kD, 40 kD or 130 kD under non-reducing conditions and 5 kD or 10-18 kD under reducing conditions, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated TRFP (Ia) comprising a first peptide chain with a sequence of 94 or 96 amino acids, fully defined in the specification, covalently linked to a second peptide chain with a sequence of 111, 109, 97 or 82 amino acids, fully defined in the specification;

(2) an isolated peptide chain (II) of TRFP comprising a sequence of 94, 96, 101, 111, 97 or 82 amino acids, fully defined in the specification;

(3) an isolated protein allergen or peptide (IIIa) capable of stimulating a T cell specific for TRFP; and

(4) an isolated protein allergen or peptide (IIIb) comprising at least one T cell epitope recognized by a T cell receptor specific for TRFP.

ACTIVITY - Antiallergic.

MECHANISM OF ACTION - Human T cell stimulator.

Peripheral blood mononuclear cells (PBMC) were purified from 60 ml of heparinized blood from 42 allergic patients. 5 ml of PBMC were cultured at 37degreesC for 6 days in the presence of 10 mug purified TRFP/ml RPMI-1640 supplemented with 5% pooled human AB serum. Viable cells were purified and cultured for 2-3 weeks at 5 units recombinant human IL-2/ml and IL-4/ml with various concentration of allergens or their fragments. Each well then received 1 muCurie tritiated thymidine for 16 hours and counted. Positive T cell proliferation greater than two times the media control was observed.

USE - TRFP is useful for reducing or preventing the adverse effects of cat allergens on cat allergic individuals and in ex vivo diagnostic tests to determine which peptides cause sensitivity so as to selectively use them to desensitize a cat sensitive individual. Purified TRFP is also useful for studying the mechanism of immunotherapy of cat allergy and to design modified derivatives, analogs or functional equivalents that are more useful in immunotherapy against cat allergy. DNA sequences encoding TRFP are useful as

probes to locate equivalent sequences present in other species (goats, sheep, dogs, rabbits or horses) that may be useful in diagnostics and/or therapeutics.

ADVANTAGE - Fully defined and characterized TRFP provides complete and a very simple desensitization therapy. MANUAL CODE: CPI: B04-N02; B14-G02A; C04-N02; C14-G02A; D05-H09; D05-H12A; D05-H12D1; D05-H17A5

TECH BIOTECHNOLOGY - Preparation: (Ia), (II),(IIIa) and (IIIb) are produced by recombinant expression of nucleic acids encoding the peptide chain (claimed).

Preferred Characteristics: (I), (Ia) or (II) has a mean human T cell stimulation index of at least 4.0 and a positivity index of at least 250 in an in vitro proliferation assay of T cell obtained from a population of TRFP sensitive individuals.

Preferred Proteins: (IIIa) and (IIIb) comprises (II) and are specific to human T cells. They may also comprise at least one B cell epitope recognized by a B cell receptor specific for TRFP.

ABEX ADMINISTRATION - A composition comprising TRFP can be administered through subcutaneous, intranasal, transdermal, oral or rectal routes. No dosage range is given.

SPECIFIC PROTEINS - The first peptide chain of (I) comprises a fully defined sequence of 94 or 96 amino acids. The second peptide chain of (I) comprises 111, 109, 97 or 82 amino acid sequences, all fully defined in the specification (claimed).

SPECIFIC SEQUENCES - The nucleotide sequence encoding the first peptide chain of (I) comprises 418 or 420 base pairs. The nucleotide sequence encoding second peptide chain of (I) comprises 476, 469 or 465 base pairs (claimed). All sequences are fully defined in the specification.

EXAMPLE - A first strand cDNA of T cell reactive feline protein (TRFP) chain 1 was synthesized with 1 mug of poly A plus RNA isolated from a pooled sample of cat parotid and mandibular glands using the EDT primer with Superscript reverse transcriptase and amplified. First strand cDNA of TRFP chain 2 was synthesized using oligo (dT) priming of mRNA prepared from a pool of the parotid/mandibular glands of five cats. An internal sequence of chain 2 was determined and PCR amplified. The carboxy terminus of the chain 2 cDNA encoding cDNA was synthesized and PCR amplified. The amplified fragments were cloned and sequenced to give carboxy terminus of chain2. NH2 terminal of TRFP chain 1 was synthesized using oligomer 5-GGGCTCGAGCTGCAGTTCTTCAGTATTCTGGCA-3' and amplified. cDNA clones encoding all or parts of TRFP chain 1 or chain 2 were subcloned into Escherichia coli expression vectors pSEM-1 carrying a truncated form of the lacZ gene. cDNA clones encoding chain1 and chain2 were altered using PCR methods so that 5 end possessed an inframe poly-histidine sequence followed by an asp-pro acid-sensitive bond. Cultures containing TRFP expression constructs produced recombinant fusion protein products upon IPTG induction which were then purified.

L69 ANSWER 18 OF 32 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1997-535583 [49] WPIX
DOC. NO. CPI: C1997-171229 [49]
DOC. NO. NON-CPI: N1997-445882 [49]
TITLE: Human monoclonal antibody specific for the AgGM4 melanoma antigen - used for diagnosis and immuno:therapy of cancer
DERWENT CLASS: B04; D16; S03
INVENTOR: GLASSY M C; MCKNIGHT M E
PATENT ASSIGNEE: (NOVO-N) NOVOPHARM BIOTECH INC
COUNTRY COUNT: 19

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC | |
|---|---|---|---|---|---|---|---|
| WO 9739774 | A1 | 19971030 | (199749)* | EN | 60[4] | | <-- |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 9739774 A1 | | WO 1997-US6665 | 19970423 |

PRIORITY APPLN. INFO: US 1996-636387 19960423
INT. PATENT CLASSIF.:
IPC RECLASSIF.: A61K0038-00 [N,A]; A61K0038-00 [N,C]; C07K0016-18 [I,C]; C07K0016-30 [I,A]; G01N0033-574 [I,A]; G01N0033-574 [I,C]

BASIC ABSTRACT:

WO 1997039774 A1 UPAB: 20050519

A human monoclonal antibody (MAb) that binds to the AgGM4 melanoma-associated antigen, termed GM4-IgG4.λ, is new. Also new are: (1) a continuous hybridoma cell line that secretes a MAb having a 129 amino acid (aa) light chain and a 144 aa heavy chain (both given in the specification, together with cDNA sequences encoding them); (2) an anti-idiotypic Ab (AAb) to GM4-IgG4.λ; (3) a purified AgGM4 antigen; (4) a nucleic acid (I) encoding a polypeptide (A) with the immunological activity of the MAb GM4-IgGλ, and containing at least 5 consecutive aas from a variable region of this antibody; (5) an expression vector containing (I); (6) a host cell containing (I); (7) (A), or fusion polypeptides containing it; and (8) polymeric forms of (A).

USE - The MAb and its fragments can be labelled and used in specific binding assays for diagnosis of melanoma, either in vivo or in vitro. The MAb can also be used for immunotherapy of malignant disease, especially melanoma. The AAb are also useful for treating malignant disease. (I) and (A) are useful in vaccines for treatment of cancer (melanoma, neuroblastoma, glioma, soft tissue sarcoma or small cell carcinoma), e.g. in patients with clinically detectable disease or those treated so that disease is not longer clinically detectable, also for palliative use (all claimed).

MANUAL CODE: CPI: B04-E02F; B04-F01; B04-F05; B04-G21; B12-K04A1; B14-H01; D05-H11A1; D05-H12A; D05-H12E; D05-H14; D05-H15; D05-H17A5; D05-H17C1
EPI: S03-E14H4

L69 ANSWER 19 OF 32 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1996-230555 [23] WPIX
DOC. NO. CPI: C1996-072878 [23]
TITLE: Peptide immunogen useful in treatment of allergy - comprises membrane-bound IgE epsilon-chain peptide synthesised linearly in tandem with T helper epitope peptide
DERWENT CLASS: B04; D16
INVENTOR: WALFIELD A M; WANG C Y
PATENT ASSIGNEE: (UNBI-N) UNITED BIOMEDICAL INC
COUNTRY COUNT: 21

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC | |
|---|---|---|---|---|---|---|---|
| WO 9612740 | A1 | 19960502 | (199623)* | EN | 53[0] | | <-- |

| | | | | | |
|---|---|---|---|---|---|
| AU 9540120 | A | 19960515 (199634) | EN | | <-- |
| EP 787150 | A1 | 19970806 (199736) | EN | [0] | <-- |
| CN 1167491 | A | 19971210 (200165) | ZH | | <-- |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 9612740 A1 | | WO 1995-US13841 | 19951025 |
| AU 9540120 A | | AU 1995-40120 | 19951025 |
| CN 1167491 A | | CN 1995-196496 | 19951025 |
| EP 787150 A1 | | EP 1995-938912 | 19951025 |
| EP 787150 A1 | | WO 1995-US13841 | 19951025 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| AU 9540120 A | Based on | WO 9612740 A |
| EP 787150 A1 | Based on | WO 9612740 A |

PRIORITY APPLN. INFO: US 1994-328519 19941025
INT. PATENT CLASSIF.:
IPC RECLASSIF.: A61K0038-00 [N,A]; A61K0038-00 [N,C]; A61K0039-00 [I,A]; A61K0039-00 [I,C]; C07K0014-005 [I,C]; C07K0014-02 [I,A]; C07K0014-12 [I,A]; C07K0016-00 [I,A]; C07K0016-00 [I,C]

BASIC ABSTRACT:

WO 1996012740 A1 UPAB: 20060110

Peptide immunogens (I) of formula (A)n-(Th)m-(B)o-(mIGE peptide) and (mIgE peptide)-(B)p-(Th)m-(A)n are new, in which A is an amino acid (AA), α-NH2, a fatty acid or its derivative or an invasin domain having immune stimulatory property; B is an AA; Th is a helper T cell epitope or its immune enhancing analogue or segment; mIgE peptide is a 26 or 17 AA sequence of formula Gly-Leu-Ala-Gly-Gly-Ser-Ala- Gln-Ser-Gln-Arg-Ala-Pro-Asp-Arg-Val-Leu-Cys-His-Ser-Gly-Gln-Gln-Gln-Gly- Leu or Pro-Glu-Leu-Asp-Val-Cys-Val-Glu-Glu-Ala-Glu-Gly-Glu-Ala-Pro-Trp- Thr resp, or is an immunogenic analogue of it; n is 1-10; m is 1-4; and o is 0-10. Also claimed are: (1) a vaccine comprising (I); and (2) a method of treating allergic reactions using (I).

USE - (I) may be used in the immunotherapeutic treatment of allergenic reactions, e.g. allergic rhinitis, food allergies, anaphylaxis or (virally-induced) asthma.

ADVANTAGE - (I) may overcome the short effective period of antihistamines, decongestants and β2 agonists, while preventing the broad immunosuppression of corticosteroids. (I) do not have the potential side effects of restlessness or sedation (antihistamines), associated increased morbidity in asthmatics (βa agonists) and adverse hormonal activities (corticosteroids).

MANUAL CODE: CPI: B04-N04; B14-G02A; B14-S11; D05-H07

=> d l69 20-32 ibib ab ind

L69 ANSWER 20 OF 32 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 1998139459 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9473230
TITLE: Apoptosis of malignant human B cells by ligation of CD20 with monoclonal antibodies.
AUTHOR: Shan D; Ledbetter J A; Press O W
CORPORATE SOURCE: Department of Biological Structure, University of Washington, Seattle, WA 98195, USA.

CONTRACT NUMBER: R01 CA55596 (NCI)
SOURCE: Blood, (1998 Mar 1) Vol. 91, No. 5, pp. 1644-52.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 26 Mar 1998
Last Updated on STN: 26 Mar 1998
Entered Medline: 16 Mar 1998

AB CD20 is a nonglycosylated 33 to 37 kD phosphoprotein involved in B -cell signaling that subserves important functions in the regulation of B-cell proliferation and differentiation. In addition, this B-cell surface antigen has been shown recently to be an effective target for immunotherapy of B-cell malignancies using chimeric (mouse/human) or radiolabeled murine monoclonal anti- CD20 antibodies. In this report we show that extensive crosslinking of CD20 with murine anti-CD20 monoclonal antibodies (MoAbs) in the presence of either goat anti-mouse IgG or Fc receptor (FcR)-expressing cells directly inhibits B-cell proliferation, induces nuclear DNA fragmentation, and leads to cell death by apoptosis. The apoptotic effects of these MoAbs can be inhibited by chelation of extracellular or intracellular Ca2+ by EGTA or Bapta AM, indicating that anti-CD20 -mediated apoptosis may be related to changes in Ca2+ concentration. These findings suggest that ligation of CD20 in vivo by anti- CD20 antibodies in the presence of FcR-expressing cells may initiate signal transduction events that induce elevation of [Ca2+]i and lead to apoptosis of malignant B cells, thereby contributing to the impressive tumor regressions observed in mouse models and clinical trials using anti-CD20 MoAbs.

CT Animals
Antibodies, Anti-Idiotypic: PD, pharmacology
*Antibodies, Monoclonal: PD, pharmacology
Antigens, CD20: IM, immunology
*Antigens, CD20: PH, physiology
*Apoptosis
*B-Lymphocytes: IM, immunology
B-Lymphocytes: PH, physiology
*Burkitt Lymphoma: PA, pathology
Calcium: ME, metabolism
Cell Cycle
Cell Division
Chelating Agents: PD, pharmacology
Cross-Linking Reagents
Egtazic Acid: AA, analogs & derivatives
Egtazic Acid: PD, pharmacology
Goats
Humans
Mice
Receptors, Fc: PH, physiology
Tumor Cells, Cultured

RN 67-42-5 (Egtazic Acid); 7440-70-2 (Calcium); 85233-19-8 (1,2-bis(2-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid)

CN 0 (Antibodies, Anti-Idiotypic); 0 (Antibodies, Monoclonal); 0 (Antigens, CD20); 0 (Chelating Agents); 0 (Cross-Linking Reagents); 0 (Receptors, Fc)

L69 ANSWER 21 OF 32 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1999044783 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9829318

TITLE: Large-scale production of CD4+ T cells from HIV-1-infected donors after CD3/CD28 costimulation.
AUTHOR: Levine B L; Cotte J; Small C C; Carroll R G; Riley J L; Bernstein W B; Van Epps D E; Hardwick R A; June C H
CORPORATE SOURCE: Immune Cell Biology Program, Naval Medical Research Institute, Bethesda, MD 20889, USA.
SOURCE: Journal of hematotherapy, (1998 Oct) Vol. 7, No. 5, pp. 437-48.
Journal code: 9306048. ISSN: 1061-6128.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 23 Feb 1999
Last Updated on STN: 23 Feb 1999
Entered Medline: 10 Feb 1999

AB We describe a procedure for large-scale enrichment, growth, and harvesting CD4+ T cells. This method may be effective for HIV-1 immunotherapy, as the mode of stimulation, with anti-CD3 plus anti-CD28 coated beads (CD3/CD28 beads) induces a potent antiviral effect. PBMC were obtained by density gradient centrifugation of an apheresis product. Monocytes/macrophages were removed by incubating PBMC with beads coated with IgG. The cells were then magnetically depleted of B cells and CD8+ cells with mouse anti-CD20 and anti-CD8 MAbs and sheep antimouse coated beads. The remaining cells were >80% CD4+ and were transferred to gas-permeable bags containing CD3/CD28 beads and cultured in a closed system. After 14 days, the cell number increased an average of 37-fold, and cells were nearly 100% CD4+. Viral load, assessed by DNA PCR for HIV-1 gag, decreased >10-fold during culture in the absence of antiretroviral agents. Removal of CD3/CD28 beads from the cell suspension was accomplished by passing cells plus beads (3-30 x 10(9) cells in 2-12 L) over a MaxSep magnetic separator using gravity-driven flow. The cells were then concentrated to 300 ml in an automated centrifuge. This process allows safe and efficient growth of large numbers of CD4+ T cells from HIV-1+ donors.

CT *Adoptive Transfer: MT, methods
Animals
Antigens, CD28: IM, immunology
Antigens, CD3: IM, immunology
CD4-Positive T-Lymphocytes: IM, immunology
*CD4-Positive T-Lymphocytes: PA, pathology
Cells, Cultured
Centrifugation, Density Gradient
HIV Infections: IM, immunology
*HIV Infections: TH, therapy
Humans
Immunosorbent Techniques
*Leukapheresis: MT, methods
Mice
CN 0 (Antigens, CD28); 0 (Antigens, CD3)

L69 ANSWER 22 OF 32 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 97265593 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9111499
TITLE: Rush immunotherapy results in allergen-specific alterations in lymphocyte function and interferon-gamma production in CD4+ T cells.
AUTHOR: Lack G; Nelson H S; Amran D; Oshiba A; Jung T; Bradley K L; Giclas P C; Gelfand E W

CORPORATE SOURCE: Department of Pediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado 80206, USA.
CONTRACT NUMBER: AI-29704 (NIAID)
HL-36577 (NHLBI)
SOURCE: The Journal of allergy and clinical immunology, (1997 Apr) Vol. 99, No. 4, pp. 530-8.
Journal code: 1275002. ISSN: 0091-6749.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 23 May 1997
Last Updated on STN: 23 May 1997
Entered Medline: 9 May 1997

AB BACKGROUND: Allergen immunotherapy results in a number of changes in clinical, inflammatory, and immunologic parameters. However, the basis for the specificity of this form of therapy is unknown, especially in the context of changes in T- and B-lymphocyte function after desensitization to specific allergens. OBJECTIVE: This study was designed to determine the immunologic consequences of rush immunotherapy. METHODS: We studied 10 patients who had positive skin test responses to the house dust mite Dermatophagoides pteronyssinus (Dpt) and cat dander extract. Each received rush immunotherapy to mite, but not cat dander, over a 2- to 4-week period until maintenance was achieved. Patients were evaluated before and when maintenance was achieved for skin test and nasal reactivity to mite and cat dander; antibody levels to the allergen were monitored, as were lymphocyte proliferative responses and cytokine production. RESULTS: Rush immunotherapy to house dust mite resulted in a significant reduction in skin and nasal reactivity to mite allergen, but not to cat allergen, in 10 of 10 patients. This was accompanied by a rise in serum anti-Dpt IgE, whereas anti-cat IgE was not altered (7 of 7 patients). In seven of seven patients there was an increase in anti-Dpt IgG4 levels. T-cell proliferative responses to mite antigen were suppressed, and numbers of CD8+ T cells increased in frequency. There was a marked increase in interferon-gamma production, particularly by CD4+ T cells in 10 of 10 patients. The correlation between the increases in interferon-gamma production and the changes in cutaneous reactivity was highly significant. CONCLUSION: We show that rush immunotherapy is immunologically specific in eliciting changes in T- and B- cell responses to the desensitization antigen. The specificity and potential benefit of immunotherapy may be linked to the increase in interferon-gamma production by allergen-activated CD4+ T lymphocytes.

CT Check Tags: Female; Male
Adolescent
*Allergens: IM, immunology
Animals
Asthma: IM, immunology
Asthma: TH, therapy
*CD4-Positive T-Lymphocytes: IM, immunology
Cats
Child
*Desensitization, Immunologic: MT, methods
Humans
Immunoglobulins: BL, blood
*Interferon Type II: BI, biosynthesis
Mites: IM, immunology
Nasal Provocation Tests: MT, methods

Skin Tests: MT, methods
RN 82115-62-6 (Interferon Type II)
CN 0 (Allergens); 0 (Immunoglobulins)

L69 ANSWER 23 OF 32 MEDLINE on STN
ACCESSION NUMBER: 94265833 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8206100
TITLE: Suppression of polyclonal and antigen-specific murine IgG1 but not IgE responses by neutralizing interleukin-6 in vivo.
AUTHOR: van Ommen R; Vredendaal A E; Savelkoul H F
CORPORATE SOURCE: Department of Immunology, Erasmus University, Rotterdam, The Netherlands.
SOURCE: European journal of immunology, (1994 Jun) Vol. 24, No. 6, pp. 1396-403.
Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 21 Jul 1994
Last Updated on STN: 3 Feb 1997
Entered Medline: 8 Jul 1994

AB The crucial role of interleukin (IL)-4 in the induction of murine IgG1 and IgE responses, which are coupled through the process of sequential isotype switching, has been well documented. Whereas IL-4 is obligatory for the induction of IgE responses, it enhances IgG1 responses. In this study, using neutralizing antibodies, we provide evidence that, besides IL-4, also IL-6 is required for obtaining peak IgG1 responses. The mRNA levels of these two cytokines are coordinately expressed in the spleen of mice immunized with trinitrophenol-keyhole limpet hemocyanin (TNP-KLH). No IL-6 requirement was observed for peak IgE responses. The IL-6 dependence of IgG1 responses was found for both antigen-specific and polyclonal responses. Moreover, it was noted using TNP-KLH and goat anti-mouse (GAM) IgD as antigen that polyclonal IgG1 responses are more dependent on IL-6 than antigen-specific responses. In vitro experiments revealed that exogenous IL-6 neither enhanced nor inhibited the IgG1 and IgE production by naive B cells , suggesting that IL-6 did not interfere with the IL-4-induced isotype switch potential. Primary and memory IgG1 responses were both similarly dependent on IL-6. These observations point to a role of IL-6 in the terminal differentiation of B cells switched to IgG1. Neutralization of IL-6 did not inhibit either antigen-specific or polyclonal IgE responses. Therefore, it was concluded that IL-6 is not involved in the terminal differentiation of B cells switched to IgE. These findings thus provide a distinct role for IL-6, besides IL-4, in regulating murine IgG1 responses. The formation of IgE, however, is completely dependent on IL-4 alone.

CT Check Tags: Female
Animals
*Antibody Specificity: IM, immunology
Enzyme-Linked Immunosorbent Assay
Hemocyanin: IM, immunology
Immunoglobulin Class Switching
Immunoglobulin D: IM, immunology
*Immunoglobulin E: IM, immunology
*Immunoglobulin G: IM, immunology
Immunotherapy, Adoptive
Interleukin-4: IM, immunology
*Interleukin-6: IM, immunology

Mice
Mice, Inbred BALB C
Nippostrongylus: IM, immunology
Polymerase Chain Reaction
RNA, Messenger: BI, biosynthesis
Spleen: CY, cytology
T-Lymphocytes: IM, immunology

RN 207137-56-2 (Interleukin-4); 37341-29-0 (Immunoglobulin E); 9013-72-3 (Hemocyanin)

CN 0 (Immunoglobulin D); 0 (Immunoglobulin G); 0 (Interleukin-6); 0 (RNA, Messenger); 0 (trinitrophenyl keyhole limpet hemocyanin)

L69 ANSWER 24 OF 32 MEDLINE on STN
ACCESSION NUMBER: 93122856 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1478708
TITLE: T-cell immunodeficiency induced by T-cell mitogens combined with cyclophosphamide injection.
AUTHOR: Kondratyeva T K; Fontalin L N; Mikheeva N V
CORPORATE SOURCE: Gamaleya Institute for Epidemiology and Microbiology, Academy of Medical Sciences, Moscow, Russia.
SOURCE: Immunology letters, (1992 Sep) Vol. 34, No. 1, pp. 71-7.
Journal code: 7910006. ISSN: 0165-2478.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199302
ENTRY DATE: Entered STN: 26 Feb 1993
Last Updated on STN: 3 Feb 1997
Entered Medline: 5 Feb 1993

AB In the murine system in vivo administration of several T- cell mitogens (LcA, Con A, anti-Thy 1.2 mAb) followed by cyclophosphamide (CP) inhibited the functional activity of T- cell subsets (Th1, Th2, Ts) but not that of B cells. T-cell counts in the spleen of treated mice proved to be significantly decreased. Conversely, T mitogens or CP alone produced a negligible effect if any. Adoptively transferred thymocytes from intact donors restored T-dependent splenocyte responses in experimental mice. In addition, it did not suppress the normal response to sheep red blood cells (SRBC). Our results indicated that the acquired immune deficiency under study is caused by polyclonal elimination (deletion) of mitogen-stimulated T cells, and could be regarded as a model of CP-induced tolerance.

CT Check Tags: Male
Animals
B-Lymphocytes: IM, immunology
Colony-Forming Units Assay
Concanavalin A: PD, pharmacology
*Cyclophosphamide: PD, pharmacology
Cytotoxicity, Immunologic
Hypersensitivity, Delayed
Immune Tolerance: DE, drug effects
*Immune Tolerance: PH, physiology
Immunity, Cellular: DE, drug effects
Immunosuppression: MT, methods
Immunotherapy, Adoptive
Isoantibodies: PD, pharmacology
Lectins: PD, pharmacology
Leukocyte Count
Lipopolysaccharides
Mice

*Mitogens: PD, pharmacology
*Plant Lectins
Spleen: CY, cytology
*T-Lymphocytes: IM, immunology
RN 11028-71-0 (Concanavalin A); 50-18-0 (Cyclophosphamide)
CN 0 (Isoantibodies); 0 (Lectins); 0 (Lipopolysaccharides); 0 (Mitogens); 0 (Plant Lectins); 0 (anti-Thy antibody); 0 (lentil lectin)

L69 ANSWER 25 OF 32 MEDLINE on STN
ACCESSION NUMBER: 90257645 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2187952
TITLE: The effect of a bacterial vaccine on tumors and the immune response of ICR/Ha mice.
AUTHOR: Havas H F; Schiffman G; Bushnell B; Dellaria M; Axelrod R S; Shanahan T; Burns M M; Guan C F
CORPORATE SOURCE: Department of Microbiology and Immunology, Temple University School of Medicine, Philadelphia, Pennsylvania 19140.
SOURCE: Journal of biological response modifiers, (1990 Apr) Vol. 9, No. 2, pp. 194-204.
Journal code: 8219656. ISSN: 0732-6580.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) .
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199006
ENTRY DATE: Entered STN: 20 Jul 1990
Last Updated on STN: 20 Jul 1990
Entered Medline: 27 Jun 1990

AB This study examined the effect of mixed bacterial vaccine (MBV), a biological response modifier prepared from Streptococcus pyogenes and Serratia marcescens, on the immune system of mice and on the regression of a transplantable mouse tumor sarcoma 37. The study examined MBV's biological properties and analyzed its chemical composition. The chemical composition varied with the growth media. A typical centrifuged, dialyzed supernate of the serum-containing preparation was found to consist mainly of protein and minimal amounts of carbohydrate and endotoxin, while MBV made with synthetic medium contained similar amounts of all three. MBV was nontoxic for mice, which gained weight following the injection of 0.5-1.0 ml of MBV. MBV caused regression of 20-100% of well-established mouse tumors without appreciable toxicity. MBV also had a striking effect on the immune response of mice to sheep red blood cells. When administered simultaneously with antigen injection, MBV increased the number of antibody-secreting splenocytes measured by the plaque-forming assay threefold. Serum antibody levels also increased two- to threefold. MBV did not enhance the immune response to pneumococcal polysaccharide type III, a B-cell-dependent response. However, the in vivo administration of MBV increased the in vitro response to MBV and the B-cell mitogen lipopolysaccharide. MBV compares favorably with other biological response modifiers because of its enhancing effect on the immune response and its oncolytic properties at nontoxic levels.

CT Animals
Bacterial Vaccines: IM, immunology
*Bacterial Vaccines: TU, therapeutic use
Bacterial Vaccines: TO, toxicity
Carbohydrates: AN, analysis
Cyclophosphamide: TU, therapeutic use
Endotoxins: AN, analysis
Hemolytic Plaque Technique
*Immunotherapy

Killer Cells, Natural: IM, immunology
Mice
Mice, Inbred ICR
Mitogens: PD, pharmacology
Neoplasm Transplantation
Proteins: AN, analysis
Sarcoma 37: IM, immunology
Sarcoma 37: PA, pathology
*Sarcoma 37: TH, therapy
*Sarcoma, Experimental: TH, therapy
*Serratia marcescens: IM, immunology
*Streptococcus pyogenes: IM, immunology
RN 50-18-0 (Cyclophosphamide)
CN 0 (Bacterial Vaccines); 0 (Carbohydrates); 0 (Endotoxins); 0 (Mitogens); 0 (Proteins)

L69 ANSWER 26 OF 32 MEDLINE on STN
ACCESSION NUMBER: 88146269 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2964111
TITLE: Selective inhibition of the canine mixed lymphocyte response by HLA-DR and DP-reactive monoclonal antibodies.
AUTHOR: Ladiges W C; Pesando J M; Severns E; Longton G; Deeg H J; Storb R
CORPORATE SOURCE: Fred Hutchinson Cancer Research Center, Seattle, Washington 98104.
CONTRACT NUMBER: CA 18221 (NCI)
CA 31787 (NCI)
RR00019 (NCRR)
+
SOURCE: Transplantation, (1988 Feb) Vol. 45, No. 2, pp. 484-8.
Journal code: 0132144. ISSN: 0041-1337.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198803
ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 29 Mar 1988

AB Twenty-three of 37 anti-Ia McAb reactive with human B cells, as determined by indirect immunocytofluorescence, were shown to be reactive with canine peripheral blood mononuclear cells (PBMC). Using a panel of human B cell lines that differ in their expression of HLA-DR, -DP, and -DQ molecules, it was shown that 15 of these antibodies identify HLA-DR and DP molecules (i.e., broadly reactive), while 22 identify only HLA-DR molecules. Fourteen of the 15 broadly reactive McAb were reactive with canine PBMC while only 9 of the 22 HLA-DR-specific McAb reacted with canine PBMC, suggesting that broadly reactive anti-Ia McAb are much more likely to react with canine cells than narrowly reactive McAb. Ten of the canine reactive McAb that were shown to identify typical Ia bimolecular structures on canine cells using immune precipitation analysis were tested for blocking activity in the canine mixed lymphocyte culture (MLC). All four of the broadly reactive McAb (B1F6, J-70, 9-49, and HB10a) plus two of the six narrowly reactive McAbs (H81.98.21 and H40.164.3) blocked the canine MLC when added to culture wells on day 0, suggesting that inhibition may be related to the specificity of the anti-Ia McAb employed. Since the MLC may reflect cellular interactions occurring during graft-versus-host disease, this assay may be useful for screening functionally relevant broadly reactive McAb in experimental canine bone marrow

transplantation studies. These data suggest that the dog may be a useful model to study anti-Ia immunotherapy.

CT Animals
*Antibodies, Monoclonal: PD, pharmacology
Antibody Specificity
Binding Sites, Antibody
*Binding, Competitive
Dogs
*HLA-D Antigens: IM, immunology
*HLA-DP Antigens: IM, immunology
*HLA-DR Antigens: IM, immunology
Humans
*Lymphocyte Culture Test, Mixed

CN 0 (Antibodies, Monoclonal); 0 (Binding Sites, Antibody); 0 (HLA-D Antigens); 0 (HLA-DP Antigens); 0 (HLA-DR Antigens)

L69 ANSWER 27 OF 32 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:259560 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200259560
TITLE: Binding to CD20 by Anti-B1 Antibody or F(ab')2 is sufficient for induction of apoptosis in B-cell lines.
AUTHOR(S): Cardarelli, Pina M. [Reprint author]; Quinn, Maire; Buckman, Dana; Fang, Yu; Colcher, David; King, David J.; Bebbington, Christopher; Yarranton, Geoffrey
CORPORATE SOURCE: Departments of Cell Biology, Molecular Biology and Biochemistry, and Radioimmunotherapy, Corixa Corporation, 600 Gateway Boulevard, South San Francisco, CA, 94080, USA
SOURCE: Cancer Immunology Immunotherapy, (March, 2002) Vol. 51, No. 1, pp. 15-24. print. CODEN: CIIMDN. ISSN: 0340-7004.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Apr 2002
Last Updated on STN: 24 Apr 2002

AB CD20 is a B-cell-specific cell surface protein expressed on mature B lymphocytes and is a target for monoclonal antibody therapy for non-Hodgkin's lymphoma (NHL). Though clear clinical efficacy has been demonstrated with several anti-CD20 antibodies, the mechanisms by which the antibodies activate CD20 and kill cells remain unclear. Proposed mechanisms of action include complement-dependent cytotoxicity (CDC), antibody-dependent cell-mediated cytotoxicity (ADCC), and induction of apoptosis. In this report we compared the activity of two anti-CD20 antibodies, Anti-B1 Antibody (tositumomab) and rituximab (C2B8), in a variety of cellular assays using a panel of B-cell lines. Anti-B1 Antibody showed a low level of activity in a CDC assay against complement-sensitive B-cell lines, Ramos and Daudi. We found that there is an inverse correlation between the expression of CD55 and CD59 and CDC mediated by either Anti-B1 Antibody or rituximab. Rituximab was more potent at inducing CDC when compared to Anti-B1 Antibody. Using Raji cells as target cells and human peripheral blood leukocytes as effector cells, Anti-B1 Antibody was a potent inducer of ADCC. The activities of Anti-B1 Antibody and rituximab were nearly identical in the ADCC assay. In addition, Anti-B1 Antibody showed direct induction of apoptosis in all B-cell lines tested. In general, crosslinking Anti-B1 Antibody with a goat anti-mouse Ig did not further enhance the percentage of cells undergoing apoptosis. Importantly, a F(ab')2 fragment of Anti-B1 Antibody induced apoptosis, while the Fab fragment did not, indicating that the Fc region was not required and dimerization of CD20 may be sufficient for induction of apoptosis. In contrast, rituximab, which

binds to an overlapping epitope on CD20 with a three-fold lower affinity than Anti-B1 Antibody, did not efficiently induce apoptosis in the cell lines tested in the absence of crosslinking. In conclusion, these two anti-CD20 antibodies have overlapping, but distinct mechanisms of action on B-cell lines.

CC Cytology - Human 02508
Neoplasms - Pathology, clinical aspects and systemic effects 24004

IT Major Concepts
Tumor Biology

IT Chemicals & Biochemicals
C-2B-8 antibody: CD-20 protein binding, leukemia cell apoptosis induction, lymphoma cell apoptosis induction; F(ab')-2 fragment: CD-20 protein binding, leukemia cell apoptosis induction, lymphoma cell apoptosis induction; anti-B-1 antibody: CD-20 protein binding, leukemia cell apoptosis induction, lymphoma cell apoptosis induction

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
BALL-1 cell line: human B-cell acute lymphoblastic leukemia cell line, in-vitro immunotherapy model system
DU-DHL-4 cell line: human diffuse histiocytic lymphoma cell line, in-vitro immunotherapy model system
DU-DHL-6 cell line: human diffuse histiocytic lymphoma cell line, in-vitro immunotherapy model system
Daudi cell line: human Burkitt lymphoma cell line, in-vitro immunotherapy model system
Jurkat cell line: human T-cell leukemia cell line
Raji cell line: human Burkitt lymphoma cell line, in-vitro immunotherapy model system
Ramos cell line: human Burkitt lymphoma cell line, in-vitro immunotherapy model system
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

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ACCESSION NUMBER: 2001:332551 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100332551
TITLE: Generation of cytotoxic T-cells against minor histocompatibility antigens on canine hematopoietic precursor cells.
AUTHOR(S): Weber, M. [Reprint author]; Lange, C. [Reprint author]; Franz, M. [Reprint author]; Kremmer, E. [Reprint author]; Kolb, H.-J. [Reprint author]
CORPORATE SOURCE: Clin. Coop. Group Hematopoietic Cell Transplantation, GSF-National Research Centre for Environment and Health, University of Munich, Munich, Germany
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 308b. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jul 2001
Last Updated on STN: 19 Feb 2002

AB Adoptive immunotherapy with donor lymphocyte transfusions has been successful in the treatment of acute and chronic myeloid leukemia. The risk of severe graft-versus-host disease has suggested sensitization of donor T-cells against minor histocompatibility antigens (mHA) on hematopoietic precursor cells (HPC). We have studied the sensitization of canine T-cells against HPC by using dendritic cells (DCs) derived from lineage-negative canine marrow cells. Marrow cells were depleted of T-cells, B-cells, granulocytes and monocytes. DCs were generated from these cells in the presence of GM-CSF for 10 to 12 days, they were characterized by morphology, expression of CD1a and MHC class II, and their stimulatory capacity in mixed lymphocyte cultures (MLC). Irradiated DCs were used to generate recipient-specific CTLs. After 8 and 12 days of a bulk culture the CTLs were restimulated and after 16 days the capacity of the CTLs to suppress the growth of HPC was tested in vitro using a Delta-Assay. The measurement of HPC suppression was performed in adaptation of the delta culture (Muench MO and Moore MA, 1992) and the CML progenitor cell proliferation assay (Smit WM et al, 1998) using lineage-negative bone marrow as target cells. The target cells were plated in triplicates in a 96-well plate at cell numbers ranging from 16.000 to 125 cells per well. The growth of HPC was stimulated by the addition of 100 ng/ml SCF, 800 U/ml GM-CSF, 2 U/ml Epo, 100 ng/ml IL-3 and 3% allogeneic MLC supernatant. At the start of the Delta Assay irradiated CTLs were added to the wells in a fixed number of 10.000 cells per well resulting in effector:target cell ratios ranging from 0.6:1 to 80:1. After 4 days the 3H-thymidine uptake of the lineage-negative bone marrow cells was measured and compared to the autologous control. The results showed a high suppression of HPC growth (>90%) in 100% (12/12) of tested DLA-mismatched combinations. In DLA-identical littermates 25% (2/8) of combinations showed a high suppression (>90%), 38% (3/8) showed a moderate suppression (25%-75%) and 38% (3/8) showed no suppression (ltoreq10%). The results in the Delta-Assay were confirmed by CFU-growth in semisolid medium. Segregation analysis in canine littermates showed one way reactivity between two males indicating autosomal mHA as well as in a female to male combination suggesting a possible Y-associated mHA in the dog.

CC Neoplasms - Blood and reticuloendothelial neoplasms 24010
General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
Endocrine - General 17002
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
Immunology - General and methods 34502
Immunology - Immunopathology, tissue immunology 34508

IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Blood and Lymphatics (Transport and Circulation)

IT Parts, Structures, & Systems of Organisms
B cells: blood and lymphatics, immune system; T cells: blood and lymphatics, immune system; bone marrow: blood and lymphatics, immune system; cytotoxic T cells: blood and lymphatics, immune system, generation; dendritic cells: immune system; granulocytes: blood and lymphatics, immune system; hematopoietic precursor cells: blood and lymphatics, immune system; monocytes: blood and lymphatics, immune system

IT Diseases
acute myeloid leukemia: blood and lymphatic disease, neoplastic disease Leukemia, Myeloid (MeSH)

IT Diseases

chronic myeloid leukemia: blood and lymphatic disease, neoplastic disease
Leukemia, Myeloid, Chronic (MeSH)
IT Diseases
graft-vs-host disease: immune system disease
Graft vs Host Disease (MeSH)
IT Chemicals & Biochemicals
granulocyte-macrophage colony stimulating factor; minor histocompatibility antigens
IT Methods & Equipment
adoptive immunotherapy: therapeutic method
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Classifier
Canidae 85765
Super Taxa
Carnivora; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
dog
Taxa Notes
Animals, Carnivores, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates
RN 83869-56-1 (granulocyte-macrophage colony stimulating factor)

L69 ANSWER 29 OF 32 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 75171582 EMBASE Full-text
DOCUMENT NUMBER: 1975171582
TITLE: Specific suppression of delayed hypersensitivity: the possible presence of a suppressor B cell in the regulation of delayed hypersensitivity.
AUTHOR: Neta R.; Salvin S.B.
CORPORATE SOURCE: Dept. Microbiol., Sch. Med., Univ. Pittsburgh, Pa.15261, United States
SOURCE: Journal of Immunology, (1974) Vol. 113, No. 6, pp. 1716-1725.
CODEN: JOIMA3
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
005 General Pathology and Pathological Anatomy
LANGUAGE: English
AB Delayed hypersensitivity to purified protein antigens in incomplete Freund's adjuvant is of a transient nature in guinea pigs. This decrease in delayed reactivity can be transferred adoptively to a sensitized recipient with lymphoid cells from the spleens and peritoneal exudate of donors 8 days after sensitization with ovalbumin. When such mixtures of donor lymphoid cells are adoptively transferred at subsequent times after sensitization, the delayed hypersensitivity of the recipient is not suppressed. When a hapten protein conjugate, such as p-aminobenzoic acid azo hen egg albumin is used as a sensitizing antigen in the donor, and when the donor cells are removed at various time intervals after the decline in delayed skin tests to the carrier protein as antigen, such as 10 to 23 days after sensitization, adoptive transfer of lymphoid cells into sensitized recipients suppresses the elicitation of delayed skin hypersensitivity to the carrier. When spleen cells are compared with peritoneal exudate (PE) cells in their suppressive capacities, only the spleen cells show suppressive action. The duration of delayed responses varied inversely with the dose of the immunosuppressive drug in guinea pigs treated with varying doses of cyclophosphamide 72 hr before sensitization. In view of the observations that PE cells are an enriched source of T cells and that the particular schedule of treatment with

cyclophosphamide affects rapidly dividing cells, the suggestion is made that a suppressor B cell may regulate the activity of a T cell in the expression of delayed skin hypersensitivity.

CT Medical Descriptors:
*b lymphocyte
*t lymphocyte
*adoptive immunotherapy
*adoptive transfer
*cell culture
*conjugation
*delayed hypersensitivity
*hapten carrier complex
*lymphocyte
*lymphocyte transfer
*peritoneum exudate
*sensitization
*spleen cell
Drug Descriptors:
*antigen
*cyclophosphamide
*hapten
*ovalbumin
*protein

RN (cyclophosphamide) 50-18-0; (ovalbumin) 77466-29-6; (protein) 67254-75-5

L69 ANSWER 30 OF 32 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-37420 DRUGU T Full-text
TITLE: Therapeutic applications of monoclonal antibodies.
AUTHOR: Berger M; Shankar V; Vafai A
CORPORATE SOURCE: Univ.Emory
LOCATION: Atlanta, Ga., USA
SOURCE: Am.J.Med.Sci. (324, No. 1, 14-30, 2002) 160 Ref.
CODEN: AJMSA9 ISSN: 0002-9629
AVAIL. OF DOC.: Biologics Branch, Scientific Resources Program, Centers for Disease Control and Prevention, US Department of Health and Human Services, Atlanta, GA 30333, U.S.A. (A.V.). (e-mail: abv4@cdc.gov).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB The therapeutic applications of monoclonal antibodies (MAb) (mAb17-1A, rituximab, trastuzumab, herceptin, daclizumab, infliximab, rhuMAB-E25, murine IgM mAb E5, MSL109 Ab, palivizumab) are reviewed. Facts on the history of mAb development, Ab structure, conventional mAb production, and new approaches and development on the use of mAb are discussed. FDA regulation of therapeutic mAb, humanizing mAb, and Ab function in immunotherapy are described. The use of mAb in cancer, recombinant immunotoxins in cancer therapy, and the use of mAb in cancer radioimmunotherapy, autoimmune disease, GVHD, rheumatoid arthritis, asthma, septicemia, complications of viral infections, natural and synthetic toxins, and substance abuse are mentioned. The development of mAb that use specificity of immunological responses is one of the most successful applications of immunology to date.

AN 2002-37420 DRUGU T Full-text
T Therapeutics
20 Immunological
69 Reviews

CT [01] RITUXIMAB *TR; TRASTUZUMAB *TR; TRASTUZUMAB *TR; HERCEPTIN *TR; HERCEPTIN *TR; DACLIZUMAB *TR; INFLIXIMAB *TR; MSL-109 *TR;

PALIVIZUMAB *TR; IN-VIVO *FT; CASES *FT; REVIEW *FT; MAIN-TOPIC *FT; MONOCLONAL *FT; ANTIBODY *FT; SEROTHERAPY *FT; HUMANIZED *FT; TR *FT

L69 ANSWER 31 OF 32 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-35529 DRUGU M P Full-text
TITLE: Recombinant BCG vaccines.
AUTHOR: Ohara N; Yamada T
CORPORATE SOURCE: Univ.Nagasaki
LOCATION: Nagasaki, Jap.
SOURCE: Vaccine (19, No. 30, 4089-98, 2001) 1 Tab. 83 Ref.
CODEN: VACCDE ISSN: 0264-410X
AVAIL. OF DOC.: Nagasaki University School of Dentistry, Sakamoto 1-7-1, Nagasaki 852-8588, Japan. (e-mail: oharan@net.nagasaki-u.ac.jp).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Recombinant BCG (rBCG) vaccines are reviewed with reference to the progress of rBCG studies, virus antigens, bacterial antigens, parasite antigens, cytokines and the role of rBCG as a new vaccine against mycobacterial infectious diseases. The development of understanding of genetic systems of mycobacteria allowed the idea of using Mycobact. w and vaccae as potential recombinant vaccines. Both have been administered during human trials in immunotherapy and as vaccines for leprosy and tuberculosis. The efficacy of BCG vaccine continues to be debated. Current BCG vaccines were originally developed from Mycobact. bovis; BCG imparts inconsistent efficacy varying between 0-80%. To develop rBCG vaccines further, a great number of animal studies are needed to resolve the remaining unanswered questions. Encouraging preclinical studies suggest that clinical trials may soon be undertaken.
AN 2001-35529 DRUGU M P Full-text
M Microbiology
P Pharmacology
20 Immunological
50 Biological Response Modifiers
69 Reviews
CT TUBERCULOSIS *OC; INFECTION,BACT. *OC; LEPROSY *OC; INFECTION,BACT. *OC; IN-VIVO *FT; IN-VITRO *FT; REVIEW *FT; RECOMBINANT *FT; VACCINE *FT; ANTIGEN *FT; MYCOBACT. *FT; BOVIS *FT; VACCAE *FT; SEROTHERAPY *FT; EFFICACY *FT; DRUG-DESIGN *FT; EXPRESSION *FT; LAB.ANIMAL *FT; IMMUNOGLOBULIN *FT; IMMUNOCOMPROMISED *FT; BORDETELLA *FT; BURGDORFERI *FT; IMMUNE-RESPONSE *FT; IMMUNIZATION *FT; VACCINATION *FT; BACT. *FT; GRAM-POS. *FT; BACT. *FT; GRAM-NEG. *FT; IMMUNITY *FT
[01] TUBERCULOSIS-VACCINE *PH; TUBERCULV *RN; MAIN-TOPIC *FT; VACCINES *FT; PH *FT
[02] BCG *PH; TUBERCULOSIS-VACCINE *PH; PH *FT

L69 ANSWER 32 OF 32 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-40168 DRUGU T S Full-text
TITLE: Peptide immunotherapy.
AUTHOR: Muller U R
LOCATION: Berne, Switz.
SOURCE: Allergy (54, Suppl. 56, 45-46, 1999) 7 Ref.
CODEN: LLRGDY ISSN: 0105-4538
AVAIL. OF DOC.: No Reprint Address.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB The effectiveness of peptide immunotherapy in the treatment of 95 cat-allergic patients was investigated in a double-blind, placebo-controlled study. The peptide mixture containing 2 T- cell-reactive, 27-amino-acid sequences from chain I of the major cat allergen FEL d 1, reduced both nasal and lung symptoms during exposure in a cat-inhabited room. However, side-effects, including respiratory symptoms, were reported. In a 2nd experiment, peptide immunotherapy with 3 T-cell epitopes of phospholipase A2 protected 5 bee-venom-allergic individuals against a bee-sting challenge. The peptide immunotherapy was not associated with side-effects. It is suggested that peptide immunotherapy with T-cell epitopes of 1 major allergen alone may not protect all patients sufficiently. (conference abstract: Symposium on Mechanisms and Management of Allergic Disease, Hamburg, Germany, 1999).

AN 1999-40168 DRUGU T S Full-text

T Therapeutics

S Adverse Effects

3 Antiallergics

20 Immunological

35 Adverse Reactions

50 Biological Response Modifiers

64 Clinical Trials

CT [01] ALLERGY *TR; ALLERGY *AE; RESPIRATION-DISORDER *AE; CASES *FT; IN-VIVO *FT; CAT *FT; THYMOCYTE *FT; PEPTIDE *FT; DOUBLE *FT; BLIND-TEST *FT; PLACEBO *FT; EC-3.1.1.4 *FT; BEE-VENOM *FT; ANTIANAPHYLACTIC *FT; PERIPHERAL *FT; BLOOD *FT; MONONUCLEAR *FT; CELL *FT; TH1 *FT; TH2 *FT; CYTOKINE *FT; B-CELL *FT; IGE *FT; IGG4 *FT; CLIN.TRIAL *FT; IMMUNOMODULATOR *FT; LAB.ANIMAL *FT; LYMPHOCYTE *FT; PHOSPHOLIPASE-A2 *FT; IMMUNOGLOBULIN *FT; TR *FT; AE *FT

******* INVENTOR RESULTS *******

```
=> d his l42

     (FILE 'HCAPLUS' ENTERED AT 16:50:26 ON 10 JUL 2007)
L42          11 S L41 AND L28

=> d que l42
L2           27 SEA FILE=REGISTRY ABB=ON  PLU=ON  (10043-66-0/BI OR 10098-91-6/
                BI OR 23214-92-8/BI OR 50-18-0/BI OR 57-22-7/BI OR 10043-49-9/B
                I OR 11056-06-7/BI OR 14265-85-1/BI OR 14378-26-8/BI OR
                14596-37-3/BI OR 14998-63-1/BI OR 154-93-8/BI OR 15755-17-6/BI
                OR 15755-39-2/BI OR 15757-86-5/BI OR 15776-20-2/BI OR 33419-42-
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                OR 58-05-9/BI OR 59-05-2/BI OR 671-16-9/BI OR 83314-01-6/BI OR
                83869-56-1/BI OR 9001-99-4/BI)
L4               QUE  ABB=ON  PLU=ON  (ANTIGENS (2A) (CD20 OR CD(W)20)) OR
                 (ANTI (2A)(CD20 OR CD(W)20))
L5               QUE  ABB=ON  PLU=ON  (ANTIGENS (2A) (CD74 OR CD 74)) OR (
                ANTI (2A) (CD74 OR CD(W)74))
L6               QUE  ABB=ON  PLU=ON  (HLA DR (2A) ANTIGENS) OR HDA DR
L7               QUE  ABB=ON  PLU=ON  NAKED ANTIBODIES OR NAKED ANTIBODY
L14      139742 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2
L15          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RADIOLABEL? IMMUNOCONJUGATE?/O
                BI
L16      256904 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CYTOKINE/OBI OR TOXIN/OBI OR
                FUSION PROTEIN/OBI OR RNASE/OBI OR RECOMBIN? RNASE/OBI OR
                RIBONUCLEASES/OBI
L17      374269 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L14 OR L15 OR L16)
L18        7247 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L4 OR L5 OR L6 OR L7)
L28              QUE  ABB=ON  PLU=ON  AY<2003 OR PRY<2003 OR PY<2003 OR MY
                <2003 OR REVIEW/DT
L37          52 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("GOLDENBERG D"/AU OR
                "GOLDENBERG D M"/AU)
L39          43 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GOLDENBERG D M/AU
L41          14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L39 OR L37) AND (L14 OR L17
                OR L18)
L42          11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L41 AND L28


=> d his l51

     (FILE 'WPIX' ENTERED AT 16:56:33 ON 10 JUL 2007)
L51          22 S L49 OR L50

=> d que l51
L2           27 SEA FILE=REGISTRY ABB=ON  PLU=ON  (10043-66-0/BI OR 10098-91-6/
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                I OR 11056-06-7/BI OR 14265-85-1/BI OR 14378-26-8/BI OR
                14596-37-3/BI OR 14998-63-1/BI OR 154-93-8/BI OR 15755-17-6/BI
                OR 15755-39-2/BI OR 15757-86-5/BI OR 15776-20-2/BI OR 33419-42-
                0/BI OR 4346-18-3/BI OR 50-02-2/BI OR 50-24-8/BI OR 53-03-2/BI
                OR 58-05-9/BI OR 59-05-2/BI OR 671-16-9/BI OR 83314-01-6/BI OR
                83869-56-1/BI OR 9001-99-4/BI)
L4               QUE  ABB=ON  PLU=ON  (ANTIGENS (2A) (CD20 OR CD(W)20)) OR
                 (ANTI (2A)(CD20 OR CD(W)20))
L5               QUE  ABB=ON  PLU=ON  (ANTIGENS (2A) (CD74 OR CD 74)) OR (
                ANTI (2A) (CD74 OR CD(W)74))
L6               QUE  ABB=ON  PLU=ON  (HLA DR (2A) ANTIGENS) OR HDA DR
L7               QUE  ABB=ON  PLU=ON  NAKED ANTIBODIES OR NAKED ANTIBODY
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L12             QUE  ABB=ON  PLU=ON  AUTOIMMUNE DISORDER?
L14      139742 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2
L15          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RADIOLABEL? IMMUNOCONJUGATE?/O
                BI
L16      256904 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CYTOKINE/OBI OR TOXIN/OBI OR
                FUSION PROTEIN/OBI OR RNASE/OBI OR RECOMBIN? RNASE/OBI OR
                RIBONUCLEASES/OBI
L17      374269 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L14 OR L15 OR L16)
L18        7247 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L4 OR L5 OR L6 OR L7)
L26             QUE  ABB=ON  PLU=ON  B CELL
L47          82 SEA FILE=WPIX ABB=ON  PLU=ON  GOLDENBERG D M/AU
L48          59 SEA FILE=WPIX ABB=ON  PLU=ON  L47 AND (L14 OR L17 OR L18)
L49           4 SEA FILE=WPIX ABB=ON  PLU=ON  L48 AND L12
L50          22 SEA FILE=WPIX ABB=ON  PLU=ON  L48 AND L26
L51          22 SEA FILE=WPIX ABB=ON  PLU=ON  L49 OR L50


=> d his l67

    (FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, DRUGU, PASCAL' ENTERED AT
    17:04:51 ON 10 JUL 2007)
L67          21 S L66 NOT L57

=> d que l67
L2           27 SEA FILE=REGISTRY ABB=ON  PLU=ON  (10043-66-0/BI OR 10098-91-6/
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                14596-37-3/BI OR 14998-63-1/BI OR 154-93-8/BI OR 15755-17-6/BI
                OR 15755-39-2/BI OR 15757-86-5/BI OR 15776-20-2/BI OR 33419-42-
                0/BI OR 4346-18-3/BI OR 50-02-2/BI OR 50-24-8/BI OR 53-03-2/BI
                OR 58-05-9/BI OR 59-05-2/BI OR 671-16-9/BI OR 83314-01-6/BI OR
                83869-56-1/BI OR 9001-99-4/BI)
L4              QUE  ABB=ON  PLU=ON  (ANTIGENS (2A) (CD20 OR CD(W)20)) OR
                 (ANTI (2A)(CD20 OR CD(W)20))
L5              QUE  ABB=ON  PLU=ON  (ANTIGENS (2A) (CD74 OR CD 74)) OR (
                ANTI (2A) (CD74 OR CD(W)74))
L6              QUE  ABB=ON  PLU=ON  (HLA DR (2A) ANTIGENS) OR HDA DR
L7              QUE  ABB=ON  PLU=ON  NAKED ANTIBODIES OR NAKED ANTIBODY
L8              QUE  ABB=ON  PLU=ON  SHEEP OR GOAT OR HORSE OR CATTLE OR
                ALPACA OR PIG OR DOG OR CAT
L9              QUE  ABB=ON  PLU=ON  RADIOLABEL? IMMUNOCONJUGATE?
L10             QUE  ABB=ON  PLU=ON  CYTOKINE OR TOXIN OR FUSION PROTEIN
                OR RNASE OR RECOMBIN? RNASE OR RIBONUCLEASES
L11             QUE  ABB=ON  PLU=ON  IMMUNOTHERAP?
L13             QUE  ABB=ON  PLU=ON  (DOMESTIC OR COMPANION) (2A) (ANIMAL
                )
L14      139742 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2
L15          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RADIOLABEL? IMMUNOCONJUGATE?/O
                BI
L16      256904 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CYTOKINE/OBI OR TOXIN/OBI OR
                FUSION PROTEIN/OBI OR RNASE/OBI OR RECOMBIN? RNASE/OBI OR
                RIBONUCLEASES/OBI
L17      374269 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L14 OR L15 OR L16)
L18        7247 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L4 OR L5 OR L6 OR L7)
L19      204919 SEA FILE=HCAPLUS ABB=ON  PLU=ON  B CELL/OBI OR T CELL/OBI OR
                MYELOID CELL/OBI OR MAST CELL/OBI OR PLASMA CELL/OBI
L20      316123 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SHEEP/OBI OR GOAT/OBI OR
                HORSE/OBI OR CATTLE/OBI OR ALPACA/OBI OR PIG/OBI OR DOG/OBI OR
                CAT/OBI
L21        1953 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 (L) L20
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L22          286 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21 AND (L17 OR L18)
L26              QUE  ABB=ON  PLU=ON  B CELL
L28              QUE  ABB=ON  PLU=ON  AY<2003 OR PRY<2003 OR PY<2003 OR MY
                 <2003 OR REVIEW/DT
L39           43 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GOLDENBERG D M/AU
L52         4293 SEA L22
L53          164 SEA L52 AND L11
L55          164 SEA L53 AND (L8 OR L13)
L56           21 SEA L55 AND L26
L57           19 SEA L56 AND L28
L58         1970 SEA L39
L59          408 SEA L58 AND (L14 OR L17 OR L18)
L62           78 SEA L59 AND L26
L63           22 SEA L62 AND ((L5 OR L6 OR L7))
L64           18 SEA L62 AND ((L9 OR L10))
L65           38 SEA L63 OR L64
L66           21 SEA L65 AND L28
L67           21 SEA L66 NOT L57


=> dup rem l42 l51 l67
PROCESSING COMPLETED FOR L42
PROCESSING COMPLETED FOR L51
PROCESSING COMPLETED FOR L67
L70           46 DUP REM L42 L51 L67 (8 DUPLICATES REMOVED)
                 ANSWERS '1-11' FROM FILE HCAPLUS
                 ANSWERS '12-33' FROM FILE WPIX
                 ANSWERS '34-42' FROM FILE MEDLINE
                 ANSWERS '43-44' FROM FILE BIOSIS
                 ANSWER '45' FROM FILE EMBASE
                 ANSWER '46' FROM FILE DRUGU

=> d l70 1-11 ibib ab

L70  ANSWER 1 OF 46  HCAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 6
ACCESSION NUMBER:         1995:369360  HCAPLUS  Full-text
DOCUMENT NUMBER:          122:211656
TITLE:                    Chimerization of LL2, a rapidly internalizing antibody
                          specific for B cell lymphoma
AUTHOR(S):                Leung, S. O.; Shevitz, J.; Pellegrini, M. C.; Dion, A.
                          S.; Shih, L. B.; Goldenberg, D. M.; Hansen,
                          H. J.
CORPORATE SOURCE:         Immunomedics, Inc., Morris Plains, NJ, 07950, USA
SOURCE:                   Hybridoma (1994), 13(6), 469-76
                          CODEN: HYBRDY; ISSN: 0272-457X
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB    LL2 is a murine monoclonal antibody (MAb) that has been shown to be effective
      for the diagnosis and treatment of patients with non-Hodgkin's B cell
      lymphoma.  Studies have also shown that radiolabeled murine LL2 (mLL2) or mLL2
      and fragments thereof coupled to Pseudomonas exotoxin (PE) can effectively
      target human B cell lymphoma in mice.  The authors have obtained the DNA
      sequences encoding the VK and VH domains of mLL2, an IgG2a MAb, which were
      combined with their resp. human κ and IgG1 constant region domains and
      expressed in SP2/0 cells.  Like its murine counterpart, the chimeric LL2
      (cLL2) antibody is glycosylated in the light chain variable region.
      Chimerization did not interfere with the immunoreactivity of the antibody, as
      determined by a competitive binding assay, where either antibody shows
      equivalent inhibition of the binding of its counterpart to the Raji cell
      membrane surface antigen, CD22.  Both antibodies bind and are rapidly
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internalized by Raji cells, whereas an irrelevant humanized antibody did not bind and was not internalized under similar conditions. The internalization rates of the bound murine or chimeric antibodies were nearly identical, with Ke values of 0.106 and 0.118 min-1 for mLL2 and cLL2, resp. The observed close equivalence between the murine and chimeric antibodies suggests potential advantages of the latter as a less immunogenic agent. Studies are currently underway to evaluate the chimeric antibody as a potential therapeutic immunoconjugate.

L70 ANSWER 2 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:205065 HCAPLUS Full-text
DOCUMENT NUMBER: 134:363419
TITLE: Response to radioimmunotherapy correlates with tumor pO2 measured by EPR oximetry in human tumor xenografts
AUTHOR(S): O'Hara, J. A.; Blumenthal, R. D.; Grinberg, O. Y.; Demidenko, E.; Grinberg, S.; Wilmot, C. M.; Taylor, A. M.; Goldenberg, D. M.; Swartz, H. M.
CORPORATE SOURCE: EPR Center, Department of Diagnostic Radiology, Dartmouth Medical School, Hanover, NH, 03755, USA
SOURCE: Radiation Research (2001), 155(3), 466-473
CODEN: RAREAE; ISSN: 0033-7587
PUBLISHER: Radiation Research Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The efficacy of radiation treatment depends upon local oxygen concentration We postulated that the variability in responsiveness of tumor xenografts to a fixed dose of radioimmunotherapy might be related to the tumor pO2 at the time that radioimmunotherapy was administered. We evaluated the growth of xenografts of CALU-3 tumors, a non-small cell lung carcinoma, in response to an 8.9-MBq dose of 131I-RS-7-anti-EGP-1 and correlated tumor growth rate with initial tumor pO2 measured by EPR oximetry. The greatest growth delay in response to radioimmunotherapy had the highest initial pO2, and the fastest-growing tumors had the lowest initial pO2. We then determined the dynamic effect of radioimmunotherapy on tumor pO2 by serial measurements of pO2 for 35 days after radioimmunotherapy. This information could be important for ascertaining the likelihood that a tumor will respond to addnl. doses as part of a multiple dose scheme. Serial tumor pO2 measurements may help identify a window of opportunity when the surviving tumor regions will be responsive to a second round of radioimmunotherapy or a second therapeutic modality such as chemotherapy or an antivascular agent. After radioimmunotherapy, there was an increase in tumor pO2 followed by a decrease below initial levels in most mice. Thus defined times may exist when a tumor is more or less radiosensitive after radioimmunotherapy.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L70 ANSWER 3 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:769945 HCAPLUS Full-text
DOCUMENT NUMBER: 134:82801
TITLE: Experimental Pretargeting Studies of Cancer with a Humanized anti-CEA μe Murine anti-[In-DTPA] Bispecific Antibody Construct and a 99mTc-/188Re-Labeled Peptide
AUTHOR(S): Karacay, H.; McBride, W. J.; Griffiths, G. L.; Sharkey, R. M.; Barbet, J.; Hansen, H. J.; Goldenberg, D. M.
CORPORATE SOURCE: Immunomedics Inc., Morris Plains, NJ, USA
SOURCE: Bioconjugate Chemistry (2000), 11(6), 842-854

CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of this study was to localize 99mTc and 188Re radionuclides to tumors, using a bispecific antibody (bsMAb) in a two-step approach where the radionuclides are attached to novel peptides incorporating moieties recognized by one arm of the bsMAb. A chemical cross-linked human/murine bsMAb, hMN-14 + 734 (Fab' + Fab'), anti-carcinoembryonic antigen [CEA] + anti-indium-DTPA was prepared as a prelude to constructing a fully humanized bsMAb for future clin. application. N,N'-o-Phenylenedimaleimide was used to cross-link the Fab' fragments of the two antibodies at their hinge regions. This construct was shown to be >92% pure and fully reactive with CEA and a divalent (indium)DTPA-peptide. For pretargeting purposes, a peptide, IMP-192 [Ac-Lys(In-DTPA)-Tyr-Lys(In- DTPA)-Lys(TscG-Cys-)-NH2 {TscG = 3-thiosemicarbazonylglyoxyl}], with two indium-DTPAs and a chelate for selectively binding 99mTc or 188Re, was synthesized. IMP-192 was formulated in a "single dose" kit and later radiolabeled with 99mTc (94-99%) at up to 1836 Ci/mmol and with 188Re (97%) at 459-945 Ci/mmol of peptide. [99mTc]IMP-192 was shown to be stable by extensive in vitro and in vivo testing and had no specific uptake in the tumor with minimal renal uptake. The biodistribution of the hMN-14 + murine 734 bsMAb was compared alone and in a pretargeting setting to a fully murine anti-CEA (F6) + 734 bsMAb that was reported previously. Both bsMAbs maintained their integrity and dual binding specificity in vivo, but the hMN-14 + m734 was cleared more rapidly from the blood. This coincided with an increased uptake of the hMN-14 + m734 bsMAb in the liver and spleen, suggesting an active reticuloendothelial cell recognition mechanism of this mixed species construct in naive mice. Animals bearing GW-39 human colonic cancer xenografts were injected with bsMAb (15 μg) and after allowing 24 or 72 h for the bsMAb constructs to clear from the blood (hMN-14 and murine F6 + 734, resp.), [188Re]IMP-192 (7 μCi) or [99mTc]IMP-192 (10 μCi) was injected at a bsMAb:peptide ratio of 10:1. Tumor uptake of [99mTc] or [188Re]IMP-192 was 12.6 ± 5.2 and 16.9 ± 5.5% ID/g at 3 h postinjection, resp. Tumor/nontumor ratios were between 5.6 and 23 to 1 for every major organ, indicating that early imaging with 99mTc will be possible. Radiation absorbed doses showed a 4.8-, 7.2-, and a 12.6 to 1.0 tumor to blood, kidney, and liver ratios when 188Re was used. Although this new bsMAb pretargeting approach requires further optimization, it already shows very promising targeting results for both radioimmunodetection and radioimmunotherapy of colorectal cancer.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L70 ANSWER 4 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:740236 HCAPLUS Full-text
DOCUMENT NUMBER: 132:233686
TITLE: Epithelial mucin-1 (MUC1) expression and MA5 anti-MUC1 monoclonal antibody targeting in multiple myeloma
AUTHOR(S): Burton, J.; Mishina, D.; Cardillo, T.; Lew, K.; Rubin, A.; Goldenberg, D. M.; Gold, D. V.
CORPORATE SOURCE: Garden State Cancer Center, Belleville, NJ, 07109, USA
SOURCE: Clinical Cancer Research (1999), 5(10, Suppl.), 3065s-3072s
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Multiple myeloma (MM) is the second most common hematol. cancer in the United States. It is typically incurable, even with myeloablative chemotherapy and stem-cell transplantation. The epithelial mucin-1 (MUC1) glycoprotein is expressed by normal and malignant epithelial cells but has also been shown to

be expressed by MM cells. MUC1 is a useful antigenic target in solid tumors for clin. diagnostic and therapeutic monoclonal antibody (mAb)-based approaches. The MA5 mAb, as well as other anti-MUC1 mAbs reactive with the MUC1 variable number tandem repeat domain, exhibited moderate to strong reactivity with both MM cell lines and clin. samples. To explore the biochem. nature and potential of MUC1 as an antigenic target in MM, studies were performed to: (a) compare the mRNA and the MUC1 glycoprotein species between epithelial cancer and MM cell lines; and (b) develop and use a human MM tumor xenograft model system to study the biodistribution of the MA5 mAb. MA5 mAb was strongly reactive with six of eight human MM cell lines by flow cytometry. In seven of eight MM patient samples (bone marrow and/or peripheral blood) reactivity was found in 10-90% of the cells, whereas normal control (n = 5) and leukemia and lymphoma (n = 5) cells showed only 0-6% reactivity. 125I-labeled MA5 whole-cell binding studies showed quant. similar amts. of binding between strongly pos. MM lines and high-MUC1-expressing breast carcinoma lines. MRNA expression was assessed by Northern blotting and reverse transcription-PCR. MM cell lines were pos. by both methods, with strong similarity in the sizes of the mRNAs and cDNAs that were obtained. Finally, biodistribution expts. were carried out with 131I-labeled MA5 vs. a nonbinding control 125I-labeled mAb in a s.c. MM xenograft model. Selective MM tumor uptake of the MA5 mAb was demonstrated, with a potential for delivering a tumor radiation absorbed dose of 8540 cGy/mCi of injected dose compared with 3099 cGy/mCi of tumor-absorbed dose delivered by nonspecific antibody.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L70 ANSWER 5 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:676211 HCAPLUS Full-text
DOCUMENT NUMBER: 132:11476
TITLE: Cell surface expression and metabolism of major histocompatibility complex class II invariant chain (CD74) by diverse cell lines
AUTHOR(S): Ong, G. L.; Goldenberg, D. M.; Hansen, H. J.; Mattes, M. J.
CORPORATE SOURCE: Garden State Cancer Center at the Center for Molecular Medicine and Immunology, Belleville, NJ, 07109, USA
SOURCE: Immunology (1999), 98(2), 296-302
CODEN: IMMUAM; ISSN: 0019-2805
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We previously described the processing of antibodies to CD74 (the major histocompatibility complex class II-associated invariant chain, Ii), by B-cell lymphoma cell lines. These cells expressed relatively low levels of Ii on the surface, but the mols. were rapidly internalized and replaced by new mols., so that ≈8 + 106 antibody mols. per cell were taken up per day. We herein report the results of similar studies with other cell types, namely a melanoma, a colon carcinoma, a T-cell lymphoma and B-lymphoblastoid cell lines. The melanoma and the carcinoma were treated with interferon-γ to induce high levels of the antigen. The T-cell lymphoma, HUT 78, was selected specifically because it was previously reported to lack cell surface Ii, while expressing the mol. intracellularly. However, HUT 78 displayed Ii on the cell surface, as did the other cell lines tested, and catabolism of the antibody was very fast on all of the cell lines. The capacity of four of the cell lines for cumulative antibody uptake was evaluated, using "residualizing" radiolabels, which are trapped within the cell after catabolism of the antibody to which they were conjugated. A high level of uptake was observed in all cases, although there was significant variation between the cell lines. With melanoma SK-MEL-37, the total LL1 uptake in 24 h was nearly 107 mols. per cell and the average turnover time for Ii on the cell surface was 4 min; with

carcinoma HT-29, the total LL1 uptake in 24 h was ≈106 mols. per cell, and the average turnover time for Ii on the cell surface was 27 min. Based on the cell content of mature class II antigens (αβ), these data suggest that a large fraction, or all, of immature class II mols. (αβIi) reach the cell surface before entering the peptide-loading compartment, independent of the particular cell type.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L70 ANSWER 6 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:226245 HCAPLUS Full-text
DOCUMENT NUMBER: 133:131855
TITLE: 90Y dosimetry in the nude mouse: evaluation of three dosimetry models in relation to the observed biological effects in the radioimmunotherapy of human colon cancer xenografts
AUTHOR(S): Behr, T. M.; Sgouros, G.; Sharkey, R. M.; Dunn, R. M.; Blumenthal, R. D.; Kolbert, K.; Juweid, M. E.; Siegel, J. A.; Goldenberg, D. M.
CORPORATE SOURCE: Garden State Cancer Center at the Center for Molecular Medicine and Immunology, Newark, NJ, 07103, USA
SOURCE: International Radiopharmaceutical Dosimetry Symposium, Proceedings of a Conference, 6th, Gatlinburg, Tenn., May 7-10, 1996 (1999), Meeting Date 1996, Volume 1, 257-271. Editor(s): Schlafke-Stelson, Audrey T.; Stabin, Michael G.; Sparks, Richard B. National Technical Information Service: Springfield, Va.
CODEN: 68TXAO
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Due to the long path length of high-energy β-emitters, cross-organ radiation may become an important issue in small animal models. The aim of this study, therefore, was to evaluate three different dosimetry models in relation to observed biol. effects in radioimmunotherapy (RAIT) with 90Y-labeled immunoconjugates (IgG, F(ab)2 and Fab) in nude mice. The maximum tolerated dose (MTD) of the 90Y-labeled anti-CEA MAb MN-14 (Fab, F(ab)2, and IgG), as well as the dose-limiting organ toxicities were determined in GW-39 colon cancer xenografted nude mice (s.c. or metastatic). The mice were treated without artificial support, with inhibition of the renal uptake of antibody fragments by D-lysine, with bone marrow transplantation (BMT), or with combinations of each. Blood counts, kidney and liver function parameters, histol., and tumor growth were monitored. The 90Y dosimetry was calculated based on three different model assumptions: 1) taking only self-doses into account, using S factors for spheres; 2) correcting for cross-organ irradiation according to the model of Hui et al.; and 3) using actual mouse anatomy as represented by magnetic resonance imaging (MRI) with a three-dimensional internal dosimetry package (3D-ID) developed by Sgouros et al.. Self-doses of Model 1 were not sufficient to describe the observed biol. effects, especially near organs with a high activity accretion. With Fab, rising liver enzymes were observed at injected activities ≥ 12 MBq, not explained by a self-dose of 4.3 Gy. Model 2 shows crossfire from the kidneys, resulting in an average liver dose of 2.45 Gy/MBq. With F(ab)2 fragments, only the combination of BMT and lysine increased the MTD, explained by cross-organ radiation from the kidneys to the red marrow of the lumbar spine, described only by Model 3 (marrow self-dose ≤ 5 Gy, crossfire up to 0.8 Gy/MBq). Antitumor effects correlated well with calculated doses. These data show that for understanding the biol. effects of 90Y in a mouse model, accounting for cross-organ irradiation is mandatory. The best correlation

between biol. effects and the dosimetry was obtained by the third, MRI-anatomy-based model, which also allows the description of crossfire from abdominal organs to the red marrow.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L70 ANSWER 7 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:459991 HCAPLUS Full-text
DOCUMENT NUMBER: 127:119058
TITLE: Pharmacokinetic evaluation of two monoclonal antibodies as possible immunoscintigraphy agents for pancreatic cancer in humans
AUTHOR(S): Molea, N.; Bodei, L.; Lazzeri, E.; Bacciardi, D.; Giulianotti, P. C.; Balestracci, D.; Viacava, P.; Campani, D.; Di Luca, L.; Salvadori, P. A.; Bonino, C.; Gold, D. V.; Sharkey, R. M.; Goldenberg, D. M.; Mosca, F.; Mariani, G.
CORPORATE SOURCE: Regional Center of Nuclear Medicine, Saluggia, Italy
SOURCE: Radioactive Isotopes in Clinical Medicine and Research, Proceedings of the International Badgastein Symposium, 22nd, Badgastein,Austria, Jan. 9-12, 1996 ( 1997), Meeting Date 1996, 413-416. Editor(s): Bergmann, Helmar; Kroiss, Alois; Sinzinger, Helmut. Birkhaeuser: Basel, Switz.
CODEN: 64SFA5
DOCUMENT TYPE: Conference
LANGUAGE: English
AB In this study we evaluated the biodistribution and potential usefulness for tumor immunoscintigraphy of two recently developed monoclonal antibodies (MoAbs), termed AR-3 and PAM4, in patients with pancreatic cancer. The two MoAbs were labeled with 131I, and their biodistribution and pharmacokinetics were assessed in 5 patients each. The plasma clearance curves of both MoA bs exhibited a biexponential pattern of decay, with average T1/2 values equal to 4-6h and 40-60 h, resp. for the fast and the slow components. While imaging with 131I-AR-3 was dubious or weakly pos., immunoscintigraphy with 131I-PAM4 more clearly outlined tumor lesions, both the primary site and locoregional recurrences, particularly at late times after injection (starting usually at about 72-96 h).

L70 ANSWER 8 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:459978 HCAPLUS Full-text
DOCUMENT NUMBER: 127:119053
TITLE: Radioimmunotherapy of CEA-expressing cancers: clinical results with an 131I-labeled anti-CEA monoclonal IgG1
AUTHOR(S): Behr, T. M.; Sharkey, R. M.; Juweid, M. E.; Dunn, R. M.; Vagg, R. C.; Swayne, L. C.; Siegel, J. A.; Goldenberg, D. M.
CORPORATE SOURCE: Garden State Cancer Center at the Center for Molecular Medicine and Immunology, Newark, NJ, 07103-2763, USA
SOURCE: Radioactive Isotopes in Clinical Medicine and Research, Proceedings of the International Badgastein Symposium, 22nd, Badgastein,Austria, Jan. 9-12, 1996 ( 1997), Meeting Date 1996, 295-300. Editor(s): Bergmann, Helmar; Kroiss, Alois; Sinzinger, Helmut. Birkhaeuser: Basel, Switz.
CODEN: 64SFA5
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Fifty-seven patients with CEA-expressing tumors in very advanced stages were treated with 44-268 mCi of the 131I-labeled murine anti-CEA monoclonal antibody NP-4. Differences in pharmacokinetics were found between different types of CEA-producing tumors: colorectal cancer patients cleared the antibody significantly faster from blood and whole-body than all other cancer types. The red marrow was the only dose-limiting organ; the severity of myelotoxicity was strongly related to the red marrow dose and the pretreatment (chemotherapy or external beam radiation). Tumor doses ranged from 2 to 218 cGy/mCi. Anti-tumor effects were seen in 12 out of 35 assessable patients (1 partial remission, 4 minor/mixed responses, 7 stabilizations of previously rapidly progressing disease).

L70 ANSWER 9 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:251179 HCAPLUS Full-text
DOCUMENT NUMBER: 116:251179
TITLE: Dose escalation of radioantibody in a mouse model with the use of recombinant human interleukin-1 and granulocyte-macrophage colony-stimulating factor intervention to reduce myelosuppression
AUTHOR(S): Blumenthal, R. D.; Sharkey, R. M.; Goldenberg, D. M.
CORPORATE SOURCE: Cent. Mol. Med. Immunol., Garden State Cancer Cent., Newark, NJ, 07103, USA
SOURCE: Journal of the National Cancer Institute (1992), 84(6), 399-407
CODEN: JNCIEQ; ISSN: 0027-8874
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In previous studies in a tumor-bearing hamster model, protection and rescue were demonstrated from radioantibody-induced hematopoietic toxicity by treatment with interleukin-1 (IL-1) before or after radioantibody treatment, as well as attenuation of duration of myelosuppression by administration of granulocyte-macrophage colony-stimulating factor (GM-CSF). The purpose of this study was to evaluate the ability of recombinant human IL-1 and recombinant murine GM-CSF to reduce myelosuppression and increase survival of non-tumor-bearing, female BALB/c mice while escalating the maximal tolerated dose (MTD) of radioantibody, the highest dose that results in no deaths. IL-1 was administered for 7 days at 1 + 103 U twice a day and GM-CSF starting on the same day for 12 days at a dose of 0.5 μg twice a day, alone or in combination. The doses of 131I-NP-4 IgG (anti-carcinoembryonic antigen monoclonal antibody) radioantibody used were 270, 340, and 370 μCi; the MTD in mice is 270 μCi. The 12-day schedule of cytokine administration was initiated at various times with respect to the radioantibody dose: on the same day, 6 or 3 days before radioantibody, or 3, 6, or 9 days after radioantibody. Treatment efficacy was measured by survival and white blood cell and platelet counts. A 25% increase to 340 μCi of radioantibody used alone resulted in 100% lethality within 25 days of treatment. The optimal cytokine schedule was a 21-day treatment with the combination of cytokines initiated 3 days before radioantibody. This treatment resulted in 100% survival and reduced the magnitude and duration of hematopoietic toxicity. The increase in radioantibody dose resulted in an 85-95% decrease in peripheral white blood cells and a 75-85% reduction in platelets within 14 days of radioantibody administration. Further dose escalation to 370 μCi of radioantibody used alone (37% increase above the MTD) resulted in lethality to 12% of the mice. IL-1 or GM-CSF alone was minimally effective. These studies are the first demonstration that cytokines could be used to reduce radioantibody-induced leukopenia and thrombocytopenia and to escalate the tolerated dose of radioantibody by 25%.

L70 ANSWER 10 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:178233 HCAPLUS Full-text
DOCUMENT NUMBER: 118:178233
TITLE: Evaluation of a tungsten-188/rhenium generator system as a ready source of rhenium-188 for use in radioimmunotherapy (RAIT)
AUTHOR(S): Griffiths, G. L.; Goldenberg, D. M.; Sharkey, R. M.; Knapp, F. F., Jr.; Callahan, A. P.; Tejada, G.; Hansen, H. J.
CORPORATE SOURCE: Immunomedics, Inc., USA
SOURCE: Radioactivity & Radiochemistry (1992), 3(4), 33, 36-7
CODEN: RARAE6; ISSN: 1045-845X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recent work on the fabrication and anal. of 188W/188Re generator systems, and the subsequent of use 188Re for exploratory antibody labeling, has now been further developed to a near-clinical scale. The largest generator fully investigated to date was prepared by adsorbing 40 mg (140 mCi) of sodium tungstate onto 13 g of alumina in a glass column sealed with teflon fittings. The generator was then autoclaved to ensure sterility and eluted with 20-mL vols. of sterile 0.9% sodium chloride throughout the testing period.

L70 ANSWER 11 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:154474 HCAPLUS Full-text
DOCUMENT NUMBER: 112:154474
TITLE: Use of hematopoietic growth factors to control myelosuppression caused by radioimmunotherapy
AUTHOR(S): Blumenthal, R. D.; Sharkey, R. M.; Quinn, L. M.; Goldenberg, D. M.
CORPORATE SOURCE: Cent. Mol. Med. Immunol., Univ. Med. Dent. New Jersey, Newark, NJ, 07103, USA
SOURCE: Cancer Research (1990), 50(3, Suppl.), 1003s-1007s
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Therapeutically efficacious doses of 131I-antibody result in a loss in circulating white blood cells; the granulocyte population is suppressed by 80-85% and the agranulocytes by 60-65% following 2 mCi of 131I-antibody in hamsters. The administration of 100,000 units of human recombinant interleukin 1 24 h prior to radioantibody can prevent the loss in WBC from 1 mCi of radioantibody and reduce the loss from 2 mCi of antibody. Recombinant murine granulocyte-macrophage colony-stimulating factor is also a potent stimulator of myelopoiesis and may also be useful as a method of reducing radioantibody-induced myelosuppression. The tumor uptake of radioantibody in animals treated with recombinant interleukin 1 is reduced by 30% 1 day after injection of radioantibody but returns to levels seen in animals not treated with the cytokine at 96 and 168 h. Therapeutic efficacy is not compromised by doses of interleukin 1 used to prevent myelosuppression. Therefore, the use of cytokines will permit the use of higher doses of radioantibody for greater tumor therapy with less myelotoxicity than in the absence of cytokine treatments.

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=> d l70 12-33 iall abeq tech abex
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L70  ANSWER 1 OF 46  HCAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 6
ACCESSION NUMBER:         1995:369360  HCAPLUS  Full-text
DOCUMENT NUMBER:          122:211656
TITLE:                    Chimerization of LL2, a rapidly internalizing antibody
                          specific for B cell lymphoma
AUTHOR(S):                Leung, S. O.; Shevitz, J.; Pellegrini, M. C.; Dion, A.
                          S.; Shih, L. B.; Goldenberg, D. M.; Hansen,
                          H. J.
CORPORATE SOURCE:         Immunomedics, Inc., Morris Plains, NJ, 07950, USA
SOURCE:                   Hybridoma (1994), 13(6), 469-76
                          CODEN: HYBRDY; ISSN: 0272-457X
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB    LL2 is a murine monoclonal antibody (MAb) that has been shown to be effective
      for the diagnosis and treatment of patients with non-Hodgkin's B cell
      lymphoma. Studies have also shown that radiolabeled murine LL2 (mLL2) or mLL2
      and fragments thereof coupled to Pseudomonas exotoxin (PE) can effectively
      target human B cell lymphoma in mice. The authors have obtained the DNA
      sequences encoding the VK and VH domains of mLL2, an IgG2a MAb, which were
      combined with their resp. human κ and IgG1 constant region domains and
      expressed in SP2/0 cells. Like its murine counterpart, the chimeric LL2
      (cLL2) antibody is glycosylated in the light chain variable region.
      Chimerization did not interfere with the immunoreactivity of the antibody, as
      determined by a competitive binding assay, where either antibody shows
      equivalent inhibition of the binding of its counterpart to the Raji cell
      membrane surface antigen, CD22. Both antibodies bind and are rapidly
      internalized by Raji cells, whereas an irrelevant humanized antibody did not
      bind and was not internalized under similar conditions. The internalization
      rates of the bound murine or chimeric antibodies were nearly identical, with
      Ke values of 0.106 and 0.118 min-1 for mLL2 and cLL2, resp. The observed
      close equivalence between the murine and chimeric antibodies suggests
      potential advantages of the latter as a less immunogenic agent. Studies are
      currently underway to evaluate the chimeric antibody as a potential
      therapeutic immunoconjugate.


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L70  ANSWER 12 OF 46  WPIX COPYRIGHT 2007        THE THOMSON CORP on STN
AN   2006-621629 [64]   WPIX  Full-text
DNC  C2006-191777 [64]
TI   Humanized L243 antibody binding human leukocyte antigen-DR, useful for
     treating cancer and immune disorders
DC   B04; D16
IN   CHANG C; GOLDENBERG D M; HANSEN H J; QU Z
PA   (CHAN-I) CHANG C; (GOLD-I) GOLDENBERG D M; (HANS-I) HANSEN H J; (IMMU-N)
     IMMUNOMEDICS INC; (QUZZ-I) QU Z
CYC  111
PIA  WO 2006094192   A2 20060908 (200664)* EN  124[24]
     US 20060210475  A1 20060921 (200664)  EN
ADT  WO 2006094192 A2 WO 2006-US7598 20060303; US 20060210475 A1 Provisional US
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2005-657695P 20050303; US 20060210475 A1 US 2006-368296 20060303
PRAI US 2005-657695P 20050303
US 2006-368296 20060303
AB WO 2006094192 A2 UPAB: 20061005
NOVELTY - A humanized L243 (hL243) antibody binding to an epitope of human leukocyte antigen (HLA)-DR on HLA-DR+ cells, is new.

DETAILED DESCRIPTION - A humanized L243 (hL243) antibody comprises:

(a) a heavy chain variable domain, in which the complementary determining region (CDR)1, CDR2 and CDR3 regions and framework residues 27, 38, 46, 68 and 91 of the variable domain are from the mouse monoclonal antibody mL243 heavy chain and the remainder of the immunoglobulin framework domains are from one or more human heavy chains; and/or

(b) a light chain variable domain, in which the CDR1, CDR2 and CDR3 regions and framework residues 37, 39, 48 and 49 of the variable domain are from the mouse monoclonal antibody mL243 light chain and the remainder of the immunoglobulin framework domains are from one or more human light chains, where the antibody has the ability to bind to at least one epitope of HLA-DR (human leukocyte antigen (HLA) encoded in the D region of the HLA gene cluster of major histocompatibility complex) on HLA-DR+ cells, and the antibody causes or leads to killing of the cells in a manner where neither cytotoxic addends nor immunological effector mechanisms are needed for the killing.

INDEPENDENT CLAIMS are included for the following:

(1) a pharmaceutical composition (C1) comprising the hL243 antibody;

(2) a pharmaceutical composition (C2) comprising the hL243 antibody conjugated to one or more peptides, lipids, polymeric carriers, micelles, nanoparticles or their combinations, and one or more effectors;

(3) treating (M1) a condition associated with undesired proliferation of cells expressing HLA-DR, by administering the pharmaceutical composition (C1) to a patient suffering from the disease;

(4) treating (M2) a patient using the pharmaceutical composition (C2);

(5) kit comprising the pharmaceutical composition (C2);

(6) treating (M3) a disorder in a subject, by administering to the subject, a 'naked' polyvalent protein complex, comprising three binding sites, at least one of which is composed of an hL243 variable domain, and one or more binding sites for a tumor associated antigen; and

(7) treating (M4) a condition associated with proliferation of cells expressing HLA-DR, by:

(a) administering an effective amount of a bispecific antibody or its fragment comprising at least one arm that specifically binds HLA-DR and at least one other arm that specifically binds a targetable conjugate, where the one arm that binds HLA-DR is an hL243 antibody or its fragment, and the targetable conjugate comprises a hapten moiety and a therapeutic agent, and administering the targetable conjugate to a patient with the condition;

(b) administering to a subject with the condition, an effective amount of a bispecific antibody or its fragment comprising one arm that specifically binds HLA-DR and one arm that binds to a tumor-associated antigen, where one arm that binds HLA-DR is an hL243 antibody or its fragment; or

(c) administering to a subject having the condition an effective amount of a antibody or its fragment that specifically binds HLA-DR, where the HLA-DR specific antibody is an hL243 antibody or its fragment, and administering to the subject before, after or simultaneously with the anti-HLA-DR antibody an effective amount of an antibody or its fragment that binds to a tumor-associated antigen.

ACTIVITY - Cytostatic; Immunosuppressive Muscular-Gen.; Neuroprotective; Dermatological; Metabolic; Endocrine-Gen; Antiinflammatory; Antiarthritic; Antirheumatic; Antiulcer; Gastrointestinal-Gen.; Nephrotropic; Antianemic; Nootropic.

In vivo therapeutic efficacy of humanized L243 (hL243) in a xenograft model of non-Hodgkin's lymphoma was carried out as follows. The therapeutic study was performed to compare the in vivo efficacy of hL243gamma4P and mL243

(IgG2a isotype) monoclonal antibodies, in a xenograft model of human non-Hodgkin's lymphoma. Severe combined immunodeficiency (SCID) mice were injected with 2.5x106 Raji cells. Therapy with hL243gamma4P or mL243 was initiated one day-post tumor cell administration. Both groups of mice were injected with saline or with non-specific control antibody, hMN14 had a median survival time (MST) of 17 days. All the groups of mice treated with either humanized or murine L243 had significantly improved life span compared to mice injected with saline or hMN14. In the group of animal treated with various doses of mL243 IgG2a, the cure rate was 80-100%. Treatment with various doses of hL243gamma4P resulted in a dose-response relationship, with mice receiving higher doses having better survival times.

MECHANISM OF ACTION - HLA-DR binding agent.

USE - For treating a condition associated with undesired proliferation of cells expressing HLA-DR, where the cells are lymphoid cells or solid cancer cells. The solid cancer cells are chosen from carcinomas, melanomas, sarcomas, gliomas and skin cancers. The condition is an autoimmune disease, leukemia or lymphoma, metabolic disease, neurodegenerative disease or one of immune-dysregulatory disorders. For treating disorder in a subject, where the disorder is a neoplastic, autoimmune or immune dysregulation disorder, metabolic disorder, or neurodegenerative disease (claimed), where the autoimmune disease include dermatomyositis, myasthenia gravis, systemic lupus erythematosus, Addison's disease, rheumatoid arthritis, multiple sclerosis, ulcerative colitis, IgA nephropathy, Sjogren's syndrome, pernicious anemia, etc., metabolic disease such as amyloidosis, and neurodegenerative disease such as Alzheimer's disease.

ADVANTAGE - The humanized L243 antibody specifically bind HLA-DR, inhibits proliferation of HLA-DR+ cells, induces expression and release of TNF molecules, have reduced immunogenicity compared to the corresponding murine antibodies, and causes or leads to killing of the cells in a manner where neither cytotoxic addends nor immunological effector mechanisms are needed for the killing.

DESCRIPTION OF DRAWINGS - The figure shows a graph illustrating the therapy of Raji-bearing SCID mice with murine L243 and human L243gamma4P.

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L70 ANSWER 13 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-415237 [42] WPIX
DOC. NO. CPI: C2006-131153 [42]
TITLE: New multispecific antagonist, for detecting and treating a condition, e.g. an inflammatory or immune-dysregulatory disorder, pathologic angiogenesis or cancer, or infectious disease
DERWENT CLASS: B04; D16
INVENTOR: GOLDENBERG D M; HANSEN H J
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 111

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2006063150 | A2 | 20060615 | (200642)* | EN | 80[0] | |
| US 20060140936 | A1 | 20060629 | (200643) | EN | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2006063150 A2 | | WO 2005-US44446 | 20051208 |
| US 20060140936 A1 | Provisional | US 2004-634076P | 20041208 |
| US 20060140936 A1 | | US 2005-296432 | 20051208 |

PRIORITY APPLN. INFO: US 2004-634076P 20041208
US 2005-296432 20051208

AB WO 2006063150 A2 UPAB: 20060703

NOVELTY - A multispecific antagonist that reacts specifically with at least two different targets, where the targets are selected from (A) proinflammatory effectors of the innate immune system, (B) coagulation factors, (C) complement factors and complement regulatory proteins, and (D) targets specifically associated with an inflammatory or immune-dysregulatory disorder or with a pathologic angiogenesis or cancer, is new.

DETAILED DESCRIPTION - A multispecific antagonist that reacts specifically with at least two different targets, where the targets are selected from (A) proinflammatory effectors of the innate immune system, (B) coagulation factors, (C) complement factors and complement regulatory proteins, and (D) targets specifically associated with an inflammatory or immune-dysregulatory disorder or with a pathologic angiogenesis or cancer, where the latter target is not (A), (B) or (C), and where:

(i) at least one of the targets is (A), (B) or (C);

(ii) when the multispecific antagonist comprises a single multispecific antibody, then CD74 is excluded as a target of the antagonist; and

(iii) when the multispecific antagonist comprises a combination of separate antibodies, combinations are excluded where one of the antibodies targets a B-cell antigen and the other antibody targets a T-cell, plasma cell, macrophage or inflammatory cytokine or their combinations are also excluded where one of the antibodies targets CD20 and the other antibody targets C3b or CD40.

INDEPENDENT CLAIMS are also included for:

(1) diagnosing or detecting a condition selected from an inflammatory or immune-dysregulatory disorders, a pathologic angiogenesis or cancer, or an infectious disease; and

(2) treating a condition selected from an inflammatory or immune-dysregulatory disorders, a pathologic angiogenesis or cancer, or an infectious disease.

ACTIVITY - Antiinflammatory; Cytostatic; Antimicrobial; Neuroprotective; Respiratory-Gen; Antiasthmatic; Antiarteriosclerotic; Immunomodulator; Cardiant; Anabolic; Antiseborrheic; Dermatological; Vasotropic. No biological data given.

MECHANISM OF ACTION - Multispecific antagonist; Angiogenesis inhibitor.

USE - The multispecific antagonist is useful in manufacturing a medicament for the treatment of a condition or for manufacturing an agent for the detection of a condition, where the condition is an inflammatory or immune-dysregulatory disorder, a pathologic angiogenesis or cancer, or an infectious disease, or septicemia or septic shock, an infectious disease, a neuropathy, graft versus host disease or transplant rejection, acute respiratory distress syndrome, a granulomatous disease, asthma, atherosclerosis, cachexia, a pathologic angiogenesis, cancer, a coagulopathy, acne, giant cell arteritis, or myocardial ischemia (claimed).

L70 ANSWER 14 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-591987 [60] WPIX
DOC. NO. CPI: C2005-178431 [60]
TITLE: Preparing an immunotoxin for diagnosing or treating, for e.g. cancer or infection, comprises culturing a mammalian host cell transformed with nucleic acid sequences

encoding fusion proteins containing recombinant cytotoxic RNAses

DERWENT CLASS: B04; D16

INVENTOR: CHANG C; GOLDENBERG D M; HANSEN H J; ROSSI E A; VANAMA S; CHANG C H

PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC

COUNTRY COUNT: 107

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2005080586 | A1 | 20050901 | (200560)* | EN | 56[13] | |
| US 20060014245 | A1 | 20060119 | (200607) | EN | | |
| EP 1720996 | A1 | 20061115 | (200675) | EN | | |
| AU 2005214361 | A1 | 20050901 | (200712) | EN | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2005080586 | A1 | WO 2005-US4860 | 20050214 |
| US 20060014245 | A1 Provisional | US 2004-544227P | 20040213 |
| EP 1720996 | A1 | EP 2005-723127 | 20050214 |
| US 20060014245 | A1 | US 2005-56182 | 20050214 |
| EP 1720996 | A1 | WO 2005-US4860 | 20050214 |
| AU 2005214361 | A1 | AU 2005-214361 | 20050214 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO | |
|---|---|---|---|---|
| EP 1720996 | A1 | Based on | WO 2005080586 | A |
| AU 2005214361 | A1 | Based on | WO 2005080586 | A |

PRIORITY APPLN. INFO: US 2004-544227P 20040213
US 2005-56182 20050214

AB WO 2005080586 A1 UPAB: 20051223

NOVELTY - Preparing an immunotoxin comprising culturing a mammalian host cell transformed with nucleic acid sequences encoding fusion proteins containing recombinant cytotoxic RNAses, is new.

DETAILED DESCRIPTION - Preparing an immunotoxin comprising culturing a mammalian host cell, where the host cell is transformed with a first nucleic acid sequence encoding a fusion polypeptide, where the fusion polypeptide comprises a non-mammalian ribonuclease fused to a first immunoglobulin variable domain, and a second nucleic acid sequence encoding a second polypeptide comprising a second immunoglobulin variable domain, where the first and second immunoglobulin variable domains together form an antigen binding site.

INDEPENDENT CLAIMS are also included for:

(1) an immunotoxin comprising:

(a) a fusion polypeptide, where the fusion protein comprises a non-mammalian ribonuclease fused to a first immunoglobulin variable domain; and

(b) a second polypeptide comprising a second immunoglobulin variable domain, where one of the immunoglobulin variable domains is a light chain variable domain and the other immunoglobulin variable domain is a heavy chain variable domain, where the first and second immunoglobulin variable domains together form an antigen binding site, and where the immunotoxin is glycosylated; or an immunotoxin comprising an internalizing antibody or antibody fragment fused to a cytotoxic RNAse moiety, where the cytotoxic RNAse

moiety bears an N-terminal pyroglutamate residue and is fused at its C-terminus to the N-terminus of a polypeptide comprising the light chain of the antibody or antibody fragment, and where the antibody or antibody fragment comprises separate light and heavy chains;

(2) a pharmaceutical composition comprising the above immunotoxin and a pharmaceutical carrier; and

(3) treating a disease or syndrome in a subject.

ACTIVITY - Cytostatic; Antimicrobial; Immunosuppressive.

No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The methods and composition are useful for diagnosing, preventing or treating diseases or syndromes associated with unwanted or inappropriate cell proliferation or activation, such as cancer, infection or autoimmune disorders.

L70 ANSWER 15 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-195723 [20] WPIX
DOC. NO. CPI: C2005-061951 [20]
TITLE: Heteroconjugate for treating B cell -related disease, inflammatory disease, systemic lupus erythematosus, diabetes mellitus and cirrhosis, comprises first binding arm and second binding arm having different binding specificity
DERWENT CLASS: B04; D16
INVENTOR: CHANG C; GOLDENBERG D M; HANSEN H J; HORAK E; HORAK I; HORAK I D; HSING-CHANG C; GOLDENBERG D; HANSEN H
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 107

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2005014618 | A2 | 20050217 | (200520)* | EN | 60[1] | |
| US 20050079184 | A1 | 20050414 | (200526) | EN | | |
| EP 1651663 | A2 | 20060503 | (200629) | EN | | |
| AU 2004263538 | A1 | 20050217 | (200663) | EN | | |
| JP 2007516213 | W | 20070621 | (200742) | JA | 40 | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2005014618 | A2 | WO 2004-US25840 | 20040809 |
| US 20050079184 | A1 Provisional | US 2003-493365P | 20030808 |
| AU 2004263538 | A1 | AU 2004-263538 | 20040809 |
| EP 1651663 | A2 | EP 2004-780644 | 20040809 |
| US 20050079184 | A1 | US 2004-913509 | 20040809 |
| EP 1651663 | A2 | WO 2004-US25840 | 20040809 |
| JP 2007516213 | W | WO 2004-US25840 | 20040809 |
| JP 2007516213 | W | JP 2006-523297 | 20040809 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO | |
|---|---|---|---|---|
| EP 1651663 | A2 | Based on | WO 2005014618 | A |
| AU 2004263538 | A1 | Based on | WO 2005014618 | A |
| JP 2007516213 | W | Based on | WO 2005014618 | A |

PRIORITY APPLN. INFO: US 2003-493365P 20030808
US 2004-913509 20040809

AB WO 2005014618 A2 UPAB: 20050708

NOVELTY - A heteroconjugate comprising a first binding arm and a second binding arm, is new. The first binding arm has different binding specificity from the second binding arm. The heteroconjugate inhibits growth and induces apoptosis of a disease cell and does not recruit effector cells upon binding to a target cell.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) treating a disorder, which involves administering a heteroconjugate;

(2) a pharmaceutical composition, which contains a carrier and the heteroconjugate; and

(3) diagnosing a disorder, comprising administering a diagnostic composition comprising the carrier and heteroconjugate.

ACTIVITY - Immunomodulator; Antiinflammatory; Cytostatic; Neuroprotective; Immunosuppressive; Antipsoriatic; Antiarthritic; Nootropic; Muscular-Gen.; Dermatological; Antidiabetic; Hepatotropic; Antianemic; Nephrotropic; Antiulcer; Gastrointestinal-Gen.; Respiratory-Gen.; Antiasthmatic; Muscular-Gen.

No biological data given.

MECHANISM OF ACTION - Apoptosis-Stimulator. Daudi cells were treated with bispecific antibody (hLL2xhA20) (100 microg/ml) for 24 hours. The apoptosis of cells was observed with hLL2xhA20 in a dose dependent manner. The result showed that the hLL2xhA20 was capable of simultaneously targeting CD22 and CD20 on B cells, could induce apoptosis and reduced viable population of cells without cross-linking.

USE - For treating B cell-related disease, T-cell related disease, immune dysregulation disease, acute or chronic inflammatory disease, solid cancer, hematopoietic tumor, metabolic disease, neurodegenerative disease, autoimmune disease, carcinoma, non-Hodgkin's lymphoma, human or veterinary T-cell leukemia, skin psoriasis, psoriatic arthritis, mycosis fungoides, amyloidosis, Alzheimer's disease, myasthenia gravis, systemic lupus erythematosus, diabetes mellitus, primary biliary cirrhosis, chronic active hepatitis, amyotrophic lateral sclerosis, pernicious anemia, glomerulonephritis, Crohn's disease, ulcerative colitis, psoriasis, chronic bronchitis, asthma, emphysema, myositis and polymyositis (claimed), etc.

ADVANTAGE - The heteroconjugate has reduced cytotoxicity, increased avidity and good bioavailability.

DESCRIPTION OF DRAWINGS - The figure shows graph representing the effect of bispecific antibodies on Daudi cells to induce apoptosis. (Drawing contains non-English language text).

L70 ANSWER 16 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-162980 [17] WPIX
DOC. NO. CPI: C2005-052696 [17]
TITLE: Novel anti-CD19 monoclonal antibody that binds CD19 antigen, useful for treating B-cell disease such as lymphoma, leukemia, or autoimmune disease such as myasthenia gravis, lupus nephritis, rheumatic fever, diabetes mellitus
DERWENT CLASS: B04; D16; K08
INVENTOR: GOLDENBERG D M; HANSEN H J; QU Z
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 107

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2005012493 | A2 | 20050210 | (200517)* | EN | 81[6] | |
| US 20050070693 | A1 | 20050331 | (200524) | EN | | |
| EP 1648512 | A2 | 20060426 | (200628) | EN | | |
| US 7109304 | B2 | 20060919 | (200662) | EN | | |
| US 20060257398 | A1 | 20061116 | (200677) | EN | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2005012493 | A2 | WO 2004-US24636 | 20040802 |
| US 20050070693 | A1 Provisional | US 2003-491282P | 20030731 |
| US 7109304 | B2 Provisional | US 2003-491282P | 20030731 |
| EP 1648512 | A2 | EP 2004-779636 | 20040802 |
| US 20050070693 | A1 | US 2004-903858 | 20040802 |
| US 7109304 | B2 | US 2004-903858 | 20040802 |
| EP 1648512 | A2 | WO 2004-US24636 | 20040802 |
| US 20060257398 | A1 Provisional | US 2003-491282P | 20030731 |
| US 20060257398 | A1 Div Ex | US 2004-903858 | 20040802 |
| US 20060257398 | A1 | US 2006-445410 | 20060601 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO | |
|---|---|---|---|---|
| EP 1648512 | A2 | Based on | WO 2005012493 | A |
| US 20060257398 | A1 | Div ex | US 7109304 | B |

PRIORITY APPLN. INFO: US 2003-491282P 20030731
US 2004-903858 20040802
US 2006-445410 20060601

AB WO 2005012493 A2 UPAB: 20060121

NOVELTY - A monoclonal antibody or its fragment (I) that binds a CD19 antigen, where (I) is chimeric, humanized or is fully human, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an antibody fusion protein or its fragment (II), comprising at least two MAbs or their fragments, where each of the MAbs independently is an anti-CD19 MAb of (I), or (I) and a second MAb or its fragment, where the second MAb or its fragment is other than (I);

(2) a nucleic acid (III) comprising a sequence encoding (I) or (II);

(3) an expression vector (IV) comprising (III);

(4) a host cell (V) comprising (III); and

(5) a B-cell targeting diagnostic or therapeutic conjugate (VI), comprising an antibody component bound to at least one diagnostic or at least one therapeutic agent, where the antibody component comprises (I) or (II).

ACTIVITY - Cytostatic; Immunosuppressive; Hemostatic; Muscular-Gen,; Neuroprotective; Antiinflammatory; Dermatological; Antirheumatic; Antidiabetic; Antiulcer; Gastrointestinal-Gen.; Antiarthritic; Anabolic; Hypertensive; Nephrotropic; Thyromimetic; Hepatotropic; Antiallergic; Vasotropic; Antianemic; Antipsoriatic; Endocrine-Gen. No supporting data is given.

MECHANISM OF ACTION - Evocates humoral and/or cellular immune response.

USE - (I) is useful for treating B-cell disease in a subject, which involves administering (I) formulated in a pharmaceutically acceptable vehicle. The B-cell disease is lymphoma, leukemia, or autoimmune disease such as acute idiopathic thrombocytopenic purpura, chronic idiopathic

thrombocytopenic purpura, dermatomyositis, Sydenham's chorea, myasthenia gravis, systemic lupus erythematosus, lupus nephritis, rheumatic fever, polyglandular syndromes, bullous pemphigoid, diabetes mellitus, Henoch-Schonlein purpura, post-streptococcalnephritis, erythema nodosum, Takayasu's arteritis, Addison's disease, rheumatoid arthritis, multiple sclerosis, sarcoidosis, ulcerative colitis, erythemia multiforme, IgA nephropathy, polyarteritis nodosa, ankylosing spondylitis, Goodpasture's syndrome, thromboangitisubiterans, Sjogern's syndrome, primary biliary cirrhosis, Hashimoto's thyroiditis, thyrotoxicosis, scleroderma, chronic active hepatitis, polymyositis/dermatomyositis, polychondritis, pamphigus vulgaris, Wegener's granulomatosis, membranous nephropathy, amyotrophic lateral sclerosis, tabes dorsalis, giant cell arteritis/polymyalgia, pernicious anemia, rapidly progressive glomerulonephritis, psoriasis and fibrosing alveolitis. The method further involves administering to the subject concurrently or sequentially a therapeutically effective amount of humanized, chimeric, human or murine MAb chosen from MAb reactive with CD4, CD5, CD8, CD14, CD15, CD19, CD20, CD21, CD22, CD23, CD25, CD33, CD37, CD38, CD40, CD40L, CD46, CD52, CD54, CD74, CD80, CD126, CD138, B7, MUC1, Ia, HM1.24, HLA-DR, tenascin, vascular endothelial growth factor (VEGF), PIGF, ED-B fibronectin, oncogene, oncogene product, NCA 66a-d, necrosis antigens, Ii, interleukin (IL)-2, T101, TAC, IL-6, tumor necrosis factor-related apoptosis-inducing ligand (TRAIL)-R1 (DR4) and TRAIL-R2 (DR5), formulated in a vehicle. The method further involves administering to the subject concurrently or sequentially therapeutic agent, formulated in a pharmaceutically acceptable vehicle, or a therapeutic conjugate comprising at least one MAb bound to at least one therapeutic agent. (I), (II) and (VI) are useful for treating B-cell disease or syndrome in a subject. The subject is a mammal. The mammal is a human dog or cat. (II) is useful for diagnosing or treating B- cell disease in a subject, which involves administering (II) formulated in a pharmaceutically acceptable vehicle, optionally a clearing agent and targetable conjugate reactive with (II). (IV) is useful for expressing (I) or (II), which involves transfecting a mammalian cell with (IV), and culturing the transfected cell. (VI) is useful for diagnosing a B-cell disease in a subject (all claimed).

L70 ANSWER 17 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-161238 [17] WPIX
DOC. NO. CPI: C2005-051955 [17]
DOC. NO. NON-CPI: N2005-135349 [17]
TITLE: New immunological reagent useful for treating e.g. tumor, cancer, infectious disease, autoimmune disease, cardiovascular disease
DERWENT CLASS: A96; B04; B05; C06; D16; K08; P31; S01; S03; S05
INVENTOR: GOLDENBERG D M; MCBRIDE W J; GOLDENBERG D; MCBRIDE W
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 107

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| US 20050025709 | A1 | 20050203 | (200517)* | EN | 62 | [29] |
| WO 2005021494 | A2 | 20050310 | (200519) | EN | | |
| EP 1633773 | A2 | 20060315 | (200620) | EN | | |
| AU 2004268932 | A1 | 20050310 | (200656) | EN | | |
| US 7172751 | B2 | 20070206 | (200713) | EN | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| US 20050025709 A1 | Provisional | US 2003-478403P | 20030613 |
| US 20050025709 A1 | | US 2004-866180 | 20040614 |
| AU 2004268932 A1 | | AU 2004-268932 | 20040614 |
| EP 1633773 A2 | | EP 2004-776484 | 20040614 |
| WO 2005021494 A2 | | WO 2004-US18646 | 20040614 |
| EP 1633773 A2 | | WO 2004-US18646 | 20040614 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO | |
|---|---|---|---|---|
| EP 1633773 | A2 | Based on | WO 2005021494 | A |
| AU 2004268932 | A1 | Based on | WO 2005021494 | A |

PRIORITY APPLN. INFO: US 2004-866180 20040614
US 2003-478403P 20030613

AB US 20050025709 A1 UPAB: 20060121

NOVELTY - Immunological reagent is new.

DETAILED DESCRIPTION - Immunological reagent of formula X-R1-D-T1(A)-R2(Z)-D-T1(B')-R3(Y)-NR4R5 or R1(X)-D-T1(A)-R2(Z)-D-T1(B')- R3(Y)-NR4R5 is new.

T1 = Dpr, Orn or Lys;

X = hard acid cation chelator, a soft acid cation chelator or Ac-;

R1 - R3 = covalent bond or at least one D-amino acid;

Y or Z = hard acid cation chelator, soft acid cation chelator or absent;

A and B' = haptens or hard acid cation chelators;

R4 and R5 = hard acid cation chelators, soft acid cation chelators, enzymes, therapeutic agents, diagnostic agents or H.

INDEPENDENT CLAIMS are included for:

(1) diagnosing (m1) and/or treating a disease or a condition leading to the disease involving administering a targetable construct (c1) comprising the immunological agent to a subject having the disease or the condition, where the construct containing at least one diagnostic or therapeutic cation and/or at least one chelated or chemically bound therapeutic agent, diagnostic agent or enzymes; and administering a multispecific antibody or antibody fragments to the subjects, where the multispecific antibody or antibody fragment has at least one arm which binds to a targeted tissue and at least one other arm which binds the construct;

(2) detecting (m2), identifying or treating a target cell, tissue or pathogen in a subject involving administering a targetable construct (c2) comprising the immunological agent; and administering a multispecific antibody or antibody fragment to the subject, where the multispecific antibody or antibody fragment comprises at least one arm which binds a target cell, tissue or pathogen and at least one other arm which binds (c2); and

(3) a kit for treating or identifying diseased tissues in a subject comprising a targetable construct, and a multispecific antibody or antibody fragment having at least one arm which binds a targeted tissue and at least one other arm which binds the targetable construct.

ACTIVITY - Cytostatic; Virucide; Antibacterial; Antimicrobial; Antiinflammatory; Immunosuppressive; Hemostatic; Dermatological; Muscular-Gen.; Neuroprotective; Antipyretic; Antidiabetic; Nephrotropic; Anabolic; Hypertensive; Antirheumatic; Antiarthritic; Neuroprotective; Antiulcer; Hepatotropic; Thyromimetic; Antiallergic; Vasotropic; Antianemic; Antipsoriatic; Cardiovascular-Gen.; Cardiant; Antiarteriosclerotic; Thrombolytic; Nootropic.

MECHANISM OF ACTION - None given.

USE - In a targetable construct for diagnosing and/or treating tumor, cancer (preferably leukemias, lymphomas, sarcomas, melanomas, carcinomas, gliomas, skin cancers, B-cell malignancy, B-cell lymphoma, chronic lymphatic leukemia, non-Hodgkin's lymphoma, acute lymphatic leukemias, multiple myeloma or cancer is esophageal, gastric, colonic, rectal, pancreatic, lung, breast, ovarian, urinary bladder, endometrial, cervical, testicular, renal, adrenal or liver cancer), infectious disease caused by pathogens, an inflammatory disease, autoimmune disease (e.g. acute idiopathic thrombpcytopenic purpura, chronic idiopathic thrombocytopenia purpura, dermatomyositis, Sydenham's chorea, myasthenia gravis, systemic lupus erythematosus, lupus nephritis, rheumatic fever, polyglandular syndrome, bullous pemphigoid, diabetic mellitus, Henoch-Schonlein purpura, post-streptococcalnephritis, erythema nodosurn, Takayasu's arteritis, Addison's disease, rheumatoid arthritis, multiple sclerosis, sarcoidosis, ulcerative colitis, erythema multiforme, IgA nephropathy, polyarteritis nodosa, ankylosing spondylitis, Goodpasture's syndrome, thromboangitisubiterans, Sjogren's syndrome, primary biliary cirrhosis, Hashimoto's thyroiditis, thyrotoxicosis, scleroderma, chronic active hepatitis, polymyositis/dermatomyositis, polychondritis, pamphigus vulgaris, Wegener's granulomatosis, membranous nephropathy, amyotrophic lateral sclerosis, tabes dorsalis, giant cell arteritis/polymyalgia, pernicious anemia, rapidly progressive glomerulonephritis, psoriasis and fibrosing alveolitis), cardiovascular disease (e.g. myocardial infarction, ischemic heart disease, atherosclerosis plaques, clots and emboli), metabolic disease (e.g. amyloidosis) and neurological disease (e.g. Alzheimer's disease) in subject (preferably humans, primates, equines, canines or felines (claimed). In radioimmunotherapy (RAIT) and radioimmunodetection (RAID) and MRI.

ADVANTAGE - The immunological agent binds to a targetable diagnostic or therapeutic conjugate and a flexible system which accommodates different diagnostic and therapeutic agents without alteration to the bi-specific or multi-specific antibodies.

L70 ANSWER 18 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-375092 [39] WPIX
DOC. NO. CPI: C2006-121266 [39]
DOC. NO. NON-CPI: N2006-316658 [39]
TITLE: Immunotherapy of B-cell malignancies using anti-CD22 antibodies
DERWENT CLASS: B04; D16
INVENTOR: GOLDENBERG D M
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 1

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| IN 2002000237 | I1 | 20050311 | (200639)* | EN | [0] | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| IN 2002000237 | I1 | IN 2002-DE237 | 20020315 |

PRIORITY APPLN. INFO: IN 2002-DE237 20020315
AB IN 200200237 I1 UPAB: 20060620
NOVELTY - B-Cell malignancies, such as the B -cell subtype of non-Hodgkin's lymphoma and chronic lymphocytic leukemia, are significant contributors to

cancer mortality. The response of B-cell malignancies to various forms of treatment is mixed. Traditional methods of treating B-cell malignancies, including chemotherapy and radiotherapy, have limited utility due to toxic side effects. Immunotherapy with anti- CD20 antibodies have also provided limited success. The use of antibodies that bind with the CD22 antigen, however, provides an effective means to treat B-cell malignancies such as indolent and aggressive forms of B-cell lymphomas, and acute and chronic forms of lymphatic Leukemia. Moreover, immunotherapy with anti-CD22 antibodies requires comparatively low doses of antibody protein, and can be used effectively in multimodal therapies. Image 0/0

L70 ANSWER 19 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-306647 [33] WPIX
CROSS REFERENCE: 2006-294573; 2006-306646
DOC. NO. CPI: C2006-101878 [33]
TITLE: Composition useful for treating autoimmune disease such as acute idiopathic thrombocytopenic purpura, diabetes mellitus, or rheumatoid arthritis, comprises at least one antibody to a B-cell antigen
DERWENT CLASS: B04; D16
INVENTOR: GOLDENBERG D M; HANSEN H J
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 1

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| AU 2005220212 | A1 | 20051103 | (200633)* | EN | 34 | [0] |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| AU 2005220212 | A1 | AU 2005-220212 | 20051006 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO | |
|---|---|---|---|---|
| AU 2005220212 | A1 | Div ex | AU 782160 | B |

PRIORITY APPLN. INFO: AU 2005-220212 20051006
AB AU 2005220212 A1 UPAB: 20060523
NOVELTY - A composition comprises a carrier and at least one antibody to a B-cell antigen.

ACTIVITY - Antiinflammatory; Dermatological; Immunosuppressive; Antipyretic; Antirheumatic; Hemostatic; Anticonvulsant; Muscular-Gen; Antiarthritic; Neuroprotective; Antiinflammatory; Antiulcer; Gastrointestinal-Gen.; Nephrotropic; Immunosuppressive; Antithyroid; Antiallergic; Antianemic; Antidiabetic; Vasotropic; Endocrine-Gen; Respiratory-Gen; Hepatotropic.

MECHANISM OF ACTION - CD22 binding agent; CD19 binding agent; CD20 binding agent; HLA-DR binding agent; CD74 binding agent.

USE - For treating autoimmune disease selected from acute idiopathic thrombocytopenic purpura, chronic idiopathic thrombocytopenic purpura, dennatomyositis, Sydenharn's chorea, myasthenia gravis, systemic lupus erythematosus, lupus nephritis, rheumatic fever, polyglandular syndromes, bullous pemphigoid, diabetes mellitus, Henoch-Schonlein purpura, post-streptococcal nephritis, erythema nodosum, Takayasu's arteritis, Addison's

disease, rheumatoid arthritis, multiple sclerosis, sarcoidosis, ulcerative colitis, erythema multiforme, IgA nephropathy, polyarteritis nodosa, ankylosing spondylitis, Goodpasture's syndrome, thromboangitis ubiterans, Sjogren's syndrome, primary biliary cirrhosis, Hashimoto's thyroiditis, thyrotoxicosis, scleroderma, chronic active hepatitis, polychondritis, polymyositis/dermatomyositis, pamphigus vulgaris, Wegener's granulomatosis, membranous nephropathy, amyotrophic lateral sclerosis, tabes dorsalis, giant cell arteritislpolymyalgia, pernicious anemia, rapidly progressive glomerulonephritis and fibrosing alveolitis (claimed).

ADVANTAGE - The composition does not show any adverse effect such a toxicity or serious infection.

L70 ANSWER 20 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-306646 [33] WPIX
CROSS REFERENCE: 2006-294573; 2006-306647
DOC. NO. CPI: C2006-101877 [33]
TITLE: Use of a composition comprising a carrier and antibody to a B-cell antigen to treat autoimmune disorder e.g. acute idiopathic thrombocytopenic purpura, chronic idiopathic thrombocytopenic purpura and dermatomyositis
DERWENT CLASS: B04; D16
INVENTOR: GOLDENBERG D M; HANSEN H J
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 1

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| AU 2005220211 | A1 | 20051103 | (200633)* | EN | 34 | [0] |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| AU 2005220211 | A1 | AU 2005-220211 | 20051006 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO | |
|---|---|---|---|---|
| AU 2005220211 | A1 | Div ex | AU 782160 | B |

PRIORITY APPLN. INFO: AU 2005-220211 20051006

AB AU 2005220211 A1 UPAB: 20060523

NOVELTY - Method for treating an autoimmune disorder comprises administering a composition (I) comprising a carrier and at least one antibody to a B-cell antigen to a subject.

ACTIVITY - Immunosuppressive; Hemostatic; Muscular-Gen.; Neuroprotective; Antiinflammatory; Dermatological; Antipyretic; Antirheumatic; Nephrotropic; Virucide; Antidiabetic; Antiarthritic; Antiulcer; Gastrointestinal-Gen.; Hepatotropic; Antithyroid; Antiallergic; Vasotropic; Antianemic; Anticonvulsant; Endocrine-Gen; Respiratory-Gen.

MECHANISM OF ACTION - CD22 binding agent; CD19 binding agent; CD20 binding agent; HLA-DR binding agent; CD74 binding agent.

USE - (I) is useful to treat autoimmune disease (acute idiopathic thrombocytopenic purpura, chronic idiopathic thrombocytopenic purpura, dermatomyositis, Sydenham's chorea, myasthenia gravis, systemic lupus

erythematosus, lupus nephritis, rheumatic fever, polyglandular syndromes, bullous pemphigoid, diabetes mellitus, Henoch-Schonlein purpura, post-streptococcal nephritis, erythema nodosum, Takayasu's arteritis, Addison's disease, rheumatoid arthritis, multiple sclerosis, sarcoidosis, ulcerative colitis, erythema multiforme, IgA nephropathy, polyarteritis nodosa, ankylosing spondylitis, Goodpasture's syndrome, thromboangitis obliterans, Sjogren's syndrome, primary biliary cirrhosis, Hashimoto's thyroiditis, thyrotoxicosis, scleroderma, chronic active hepatitis, polymyositis/dermatomyositis, polychondritis, pemphigus vulgaris, Wegener's granulomatosis, membranous nephropathy, amyotrophic lateral sclerosis, tabes dorsalis, giant cell arteritis/polymyalgia, pernicious anemia, rapidly progressive glomerulonephritis or fibrosing alveolitis) (claimed). The ability of (I) to treat rheumatoid arthritis was tested in human. The results showed that (I) significantly reduced the B- cells from the blood, without any infectious complications, or other drug-related toxicity.

ADVANTAGE - The method requires comparatively low doses of (I) to treat autoimmune disorder.

L70 ANSWER 21 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-294573 [31] WPIX
CROSS REFERENCE: 2006-306646; 2006-306647
DOC. NO. CPI: C2006-096464 [31]
TITLE: Composition useful for treating autoimmune disease e.g. acute idiopathic thrombocytopenic purpura; chronic idiopathic thrombocytopenic purpura; dennatomyositis comprises carrier and antibody to a B-cell antigen
DERWENT CLASS: B04; D16
INVENTOR: GOLDENBERG D M; HANSEN H J
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 1

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| AU 2005220209 | A1 | 20051103 | (200631)* | EN | 34 | [0] |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| AU 2005220209 | A1 | AU 2005-220209 | 20051006 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO | |
|---|---|---|---|---|
| AU 2005220209 | A1 | Div ex | AU 782160 | B |

PRIORITY APPLN. INFO: AU 2005-220209 20051006

AB AU 2005220209 A1 UPAB: 20060515

NOVELTY - A composition comprises a carrier and at least one antibody to a B-cell antigen.

ACTIVITY - Antiinflammatory; Dermatological; Immunosuppressive; Antipyretic; Antirheumatic; Antiarthritic; Neuroprotective; Antiinflammatory; Antiulcer; Gastrointestinal-Gen.; Nephrotropic; Immunosuppressive; Antithyroid; Antiallergic; Antianemic; Antidiabetic; Hemostatic;

Anticonvulsant; Muscular-Gen; Vasotropic; Endocrine-Gen; Respiratory-Gen; Hepatotropic;

MECHANISM OF ACTION - CD22 binding agent; CD19 binding agent; CD20 binding agent; CD74 binding agent; HLA-DR binding agent.

USE - For treating autoimmune disease selected from acute idiopathic thrombocytopenic purpura, chronic idiopathic thrombocytopenic purpura, dermatomyositis, Sydenham's chorea, myasthenia gravis, systemic lupus erythematosus, lupus nephritis, rheumatic fever, polyglandular syndromes, bullous pemphigoid, diabetes mellitus, Henoch-Schonlein purpura, post-streptococcal nephritis, erythema nodosum, Takayasu's arteritis, Addison's disease, rheumatoid arthritis, multiple sclerosis, sarcoidosis, ulcerative colitis, erythema multiforme, IgA nephropathy, polyarteritis nodosa, ankylosing spondylitis, Goodpasture's syndrome, thromboangitis obliterans, Sjogren's syndrome, primary biliary cirrhosis, Hashimoto's thyroiditis, thyrotoxicosis, scleroderma, chronic active hepatitis, polychondritis, polymyositis/dermatomyositis, pemphigus vulgaris, Wegener's granulomatosis, membranous nephropathy, amyotrophic lateral sclerosis, tabes dorsalis, giant cell arteritis/polymyalgia, pernicious anemia, rapidly progressive glomerulonephritis and fibrosing alveolitis (claimed).

ADVANTAGE - The composition does not show any adverse effect such a toxicity or serious infection.

L70 ANSWER 22 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-525807 [50] WPIX
DOC. NO. CPI: C2004-193480 [50]
TITLE: Use of therapeutic composition comprising conjugated antibody or conjugated antibody fusion protein, in manufacture of medicament for use in treating disease such as non-Hodgkin's lymphoma in mammal
DERWENT CLASS: B04; B05; C03; C06; D16; K08
INVENTOR: GOLDENBERG D M; HANSEN H; HANSEN H J
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC; (MCCA-I) MCCALL J D
COUNTRY COUNT: 106

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2004058298 | A1 | 20040715 | (200450)* | EN | 49[0] | |
| US 20040219156 | A1 | 20041104 | (200473) | EN | | |
| AU 2003295166 | A1 | 20040722 | (200476) | EN | | |
| EP 1578440 | A1 | 20050928 | (200563) | EN | | |
| CZ 2005000487 | A3 | 20051214 | (200603) | CS | | |
| BR 2003017898 | A | 20051206 | (200624) | PT | | |
| JP 2006513203 | W | 20060420 | (200627) | JA | 35 | |
| MX 2005007245 | A1 | 20050901 | (200629) | ES | | |
| KR 2005100366 | A | 20051018 | (200649) | KO | | |
| CN 1756561 | A | 20060405 | (200654) | ZH | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2004058298 | A1 | WO 2003-GB5700 | 20031231 |
| US 20040219156 | A1 Provisional | US 2002-437145P | 20021231 |
| US 20040219156 | A1 | US 2003-747199 | 20031230 |
| AU 2003295166 | A1 | AU 2003-295166 | 20031231 |
| BR 2003017898 | A | BR 2003-17898 | 20031231 |
| EP 1578440 | A1 | EP 2003-786167 | 20031231 |

| | |
|---|---|
| EP 1578440 A1 | WO 2003-GB5700 20031231 |
| CZ 2005000487 A3 | WO 2003-GB5700 20031231 |
| BR 2003017898 A | WO 2003-GB5700 20031231 |
| JP 2006513203 W | WO 2003-GB5700 20031231 |
| MX 2005007245 A1 | WO 2003-GB5700 20031231 |
| KR 2005100366 A | WO 2003-GB5700 20031231 |
| JP 2006513203 W | JP 2004-563380 20031231 |
| CZ 2005000487 A3 | CZ 2005-487 20031231 |
| KR 2005100366 A | KR 2005-712463 20050630 |
| MX 2005007245 A1 | MX 2005-7245 20050630 |
| CN 1756561 A | CN 2003-80110054 20031231 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO | |
|---|---|---|---|---|
| AU 2003295166 | A1 | Based on | WO 2004058298 | A |
| EP 1578440 | A1 | Based on | WO 2004058298 | A |
| CZ 2005000487 | A3 | Based on | WO 2004058298 | A |
| BR 2003017898 | A | Based on | WO 2004058298 | A |
| JP 2006513203 | W | Based on | WO 2004058298 | A |
| MX 2005007245 | A1 | Based on | WO 2004058298 | A |
| KR 2005100366 | A | Based on | WO 2004058298 | A |

PRIORITY APPLN. INFO: US 2002-437145P 20021231
US 2003-747199 20031230

AB WO 2004058298 A1 UPAB: 20060121

NOVELTY - Use of a therapeutic composition (I) comprising a pharmaceutically acceptable vehicle and at least one conjugated antibody, conjugated antibody fusion protein or its fragment, in the manufacture of a medicament for use in treating a disease, where predosing with a non-radiolabeled antibody is not preformed and where the therapeutic composition is concurrently and sequentially administered to mammal.

DETAILED DESCRIPTION - Use of a therapeutic composition (I) comprising:

(i) a pharmaceutically acceptable vehicle and at least one conjugated antibody or its fragment or a conjugated antibody fusion protein or its fragment,

(ii) pharmaceutically acceptable vehicle and a multispecific multivalent antibody, fragment or fusion protein conjugate that binds to at least one target antigen and a therapeutic agent, or

(iii) a multispecific multivalent antibody, fragment or fusion protein that binds to at least one target antigen, optionally, a clearing agent to allow the composition to clear non-localized antibodies from circulation, and therapeutic conjugate that binds to the multispecific multivalent antibody, fragment or fusion protein, in the manufacture of a medicament for use in treating a disease in a mammal, where predosing with a non-radiolabeled antibody is not preformed and where the therapeutic composition is concurrently and sequentially administered to the mammal.

ACTIVITY - Cytostatic; Muscular-Gen.; Neuroprotective; Antiinflammatory; Dermatological, Immunosuppressive; Antipyretic; Antirheumatic; Antidiabetic; Anabolic; Hypertensive; Antiarthritic; Neuroprotective; Antiulcer; Gastrointestinal-Gen.; Nephrotrophic; Hepatotropic; Antithyroid; Antiallergic; Vasotropic; Antianemic; Antipsoriatic; Hemostatic.

A 66-year-old man with stage IV diffuse-large cell non-Hodgkin's lymphoma (NHL), having relapsed after 3 courses of chemotherapy given in the prior two years, was given a dose of two injections of 90Y-DOTA-epratuzumab one week apart, having 7.5 mCi/m2 of 90Y administered by intravenous infusion with a total dose of 30 mg antibody protein each time. Six weeks later, the cervical lymph nodes and splenomegaly reduced markedly, and the patient was

symptomatically improved and returned to work full time. For complete remission, continuous therapy was instituted involving a combination of epratuzumab (360 mg/m2) and hA20 (250 mg/m2), given every other week for a total of 4 infusions, and then the combined antibody therapy course was repeated 12 weeks later. Three months after completion of the second therapy course with the combination of unconjugated CD22 and CD20 antibodies, the patient had no evidence of disease by radiological scans or bone marrow biopsy, and was thus considered to be a complete response.

MECHANISM OF ACTION - Immunotherapy.

USE - (I) is useful for treating B cell-related disease, T-cell related disease or autoimmune disease. The B- cell related disease is an indolent form of B- cell lymphoma such as non-Hodgkin's lymphoma, an aggressive form of B-cell lymphoma, a chronic lymphocytic leukemia, an acute lymphocytic leukemia, a Waldenstrom's macroglobulinemia, or a multiple myeloma. The B-cell related disease is a human or veterinary disease. The T-cell related disease is a human or veterinary T-cell leukemia or mycosis fungoides. The autoimmune disease is chosen from acute idiopathic thrombocytopenic purpura, chronic idiopathic thrombocytopenic purpura, dermatomyositis, Sydenham's chorea, myasthenia gravis, systemic lupus erythematosus, lupus nephritis, rheumatic fever, polyglandular syndromes, bullous pemphigoid, diabetes mellitus, Henoch-Schonlein purpura, post-streptococcal nephritis, erythema nodosum, Takayasu's arteritis, Addison's disease, rheumatoid arthritis, multiple sclerosis, sarcoidosis, ulcerative colitis, erythema multiforme, IgA nephropathy, polyarteritis nodosa, ankylosing spondylitis, Goodpasture's syndrome, thromboangitis ubiterans, Sjogren's syndrome, primary biliary cirrhosis, Hashimoto's thyroiditis, thyrotoxicosis, scleroderma, chronic active hepatitis, polymyositis/dermatomyositis, polychondritis, pamphigus vulgaris, Wegener's granulomatosis, membranous nephropathy, amyotrophic lateral sclerosis, tabes dorsalis, giant cell arteritis/polymyalgia, pernicious anemia, rapidly progressive glomerulonephritis, psoriasis, and fibrosing alveolitis (all claimed).

L70 ANSWER 23 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-010089 [01] WPIX
CROSS REFERENCE: 1999-045130; 2001-041267; 2001-122704; 2002-351262; 2003-767381
DOC. NO. CPI: C2005-002825 [01]
DOC. NO. NON-CPI: N2005-007942 [01]
TITLE: Composition useful in treating and/or diagnosing, for example, graft-versus-host disease or CD74-expressing malignancy, comprises immunoconjugate having anti -CD74 binding molecules conjugated to lipids, polymeric carriers, and effectors
DERWENT CLASS: A17; A23; A25; A96; B04; B07; D16; K08; T01
INVENTOR: GOLDENBERG D M; GRIFFITHS G L; HANSEN H J; LUNDBERG B B; GOLDENBERG D; GRIFFITHS G; HANSEN H; LUNDBERG B
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 107

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| US 20040219203 | A1 | 20041104 | (200501)* | EN | 44 | [9] |
| WO 2004110390 | A2 | 20041223 | (200502) | EN | | |
| EP 1644729 | A2 | 20060412 | (200626) | EN | | |
| AU 2004247270 | A1 | 20041223 | (200656) | EN | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| US 20040219203 | A1 Cont of | US 1999-307816 | 19990510 |
| US 20040219203 | A1 Cont of | US 2000-590284 | 20000609 |
| US 20040219203 | A1 Cont of | US 2001-965796 | 20011001 |
| US 20040219203 | A1 Provisional | US 2002-360259P | 20020301 |
| US 20040219203 | A1 CIP of | US 2002-314330 | 20021209 |
| US 20040219203 | A1 CIP of | US 2003-350096 | 20030124 |
| US 20040219203 | A1 CIP of | US 2003-377122 | 20030303 |
| US 20040219203 | A1 Provisional | US 2003-478830P | 20030617 |
| US 20040219203 | A1 | US 2003-706852 | 20031112 |
| EP 1644729 | A2 | EP 2004-776666 | 20040617 |
| WO 2004110390 | A2 | WO 2004-US19238 | 20040617 |
| EP 1644729 | A2 | WO 2004-US19238 | 20040617 |
| AU 2004247270 | A1 | AU 2004-247270 | 20040617 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO | |
|---|---|---|---|---|
| US 20040219203 | A1 | Cont of | US 6306393 | B |
| EP 1644729 | A2 | Based on | WO 2004110390 | A |
| AU 2004247270 | A1 | Based on | WO 2004110390 | A |

PRIORITY APPLN. INFO: US 2003-706852 20031112
US 1999-307816 19990510
US 2000-590284 20000609
US 2001-965796 20011001
US 2002-360259P 20020301
US 2002-314330 20021209
US 2003-350096 20030124
US 2003-377122 20030303
US 2003-478830P 20030617

AB US 20040219203 A1 UPAB: 20060121

NOVELTY - A composition (I) comprises an immunoconjugate which has one or more anti-CD74 binding molecules conjugated to one or more lipids, polymeric carriers, micelles, nanoparticles or their combinations, and one or more effectors.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) preparing (M1) a carrier, involves mixing one or more amphiphilic lipids with an effector to form a carrier, and contacting the carrier with an anti-CD744 antibody; and

(2) a kit comprising (I).

ACTIVITY - Immunosuppressive; Cytostatic; Immunomodulatory.

In vitro analysis of the cytotoxic activity of free floxuridine (FUdR) and 3',5'-O-dioleoyl-FudR (FUdR-dO)-loaded emulsions and liposomes with and without coupled LL1 was performed on Raji human B- cell lymphoma lines, as follows. The cells (4x105) were plated in 24-well plates and incubated with drug containing preparations. Control experiments included free LL1 and drug free emulsions and liposomes. Cells were incubated for 24 hours at 37degreesC in an atmosphere of 95% humidity and carbon dioxide (5%). The cells were washed twice before replacing with fresh media and incubated for an additional 48 hours. Then, tetrazolium dye was added, and formed reduction product was spun down, dissolved in EtOH:dimethyl sulfoxide (1:1) and read at 570 nm. The cytotoxic activity of FUdR-dO in LL1 conjugated emulsions and liposomes was tested and compared with the activity of unconjugated drug-carriers on Raji lymphoma cells. The result indicated an effective cytotoxic activity of FUdR-

dO in both LL1-emulsions and LL1-liposomes, when compared with FUdR, where IC70 values were 0.45, 1.25, 5.3 and 7.3 microM for FUdR-dO loaded LL1-emulsions, LL1-liposomes, emulsions and liposomes, respectively.

MECHANISM OF ACTION - Immunotoxin; Radioimmunotherapeutic.

USE - (I) is useful for treating and/or diagnosing a disease or disorder, which involves administering to a patient a therapeutic and/or diagnostic composition comprising (I), and an excipient. The disease or disorder is a CD74-expressing malignancy. The disease or disorder is chosen from an immune dysregulation disease, autoimmune disease, organ-graft rejection and graft-versus-host disease. The CD74-expressing malignancy is chosen from solid tumor, non- Hodgkin's lymphoma, Hodgkin's lymphoma, multiple myeloma, B-cell malignancy, and T-cell malignancy. The disease or disorder is CD74-expressing malignancy other than lymphoma or leukemia. The CD74-expressing malignancy is a solid tumor, which is chosen from melanoma, carcinoma, sarcoma and glioma. The carcinoma is chosen from renal carcinoma, lung carcinoma, intestinal carcinoma, stomach carcinoma, breast carcinoma, prostate cancer, ovarian cancer, and melanoma. The CD74-expressing malignancy is a B- cell malignancy chosen from indolent forms of B- cell lymphomas, aggressive forms of B-cell lymphomas, chronic lymphatic leukemias, acute lymphatic leukemias and multiple myeloma. (I) comprises LL1 or its fragment. The composition further comprises one or more additional antibodies or their fragments chosen from anti-CD19, anti-CD20, anti-CD22, anti-CD30, anti-CD33, anti-CD52, anti-human leukocyte antigen (HLA)-DR, anti-MUC1, anti-TAC and their mixtures. The one or more of the additional antibodies are conjugated to one or more of the lipids, polymeric carriers, micelles, nanoparticles or their combinations. The effector molecule comprises one or more drugs, prodrugs, toxins, enzymes, radioisotopes, immunomodulators, cytokines, hormones, antibodies, oligonucleotides or their combinations (especially where the effector is FUdr, FUdr-dO or its mixtures).

The composition may further comprise one or more agents for photodynamic therapy, where the agent for photodynamic therapy is a photosensitizer, which comprises a benzoporphyrin monoacid ring A (BDP-MA), tin etiopurpurin (SnET2), sulfonated aluminum phthalocyanine (AISPc) and lutetium texaphyrin (Lutex). The composition comprises one or more diagnostic agents. The composition comprises a diagnostic nuclide, which comprises 18F, 52Fe, 62Cu, 64Cu, 67Cu, 67Ga, 68Ga, 86Y, 89Zr, 94Tc, 94mTc, 99mTc, 111In, 123In, 123I, 124I, 125I, 131I or their mixtures. The diagnostic nuclide emits 25-4000 keV gamma particles and/or positrons. The diagnostic agent is used for performing positron emission tomography (PET). The method further involves performing PET. The diagnostic agent comprises one or more image enhancing agents and the method further involves performing magnetic resonance imaging (MRI). The image enhancing agent comprises gadolinium ions, lanthanum ions, manganese ions, iron, chromium, copper, cobalt, nickel, fluorine, dysprosium, rhenium, europium, terbium, holmium, neodymium or their mixtures. The composition comprises one or more radiopaque agents or contrast agents for X-ray or computed tomography (CT). The radiopaque or contrast agents include barium, diatrizoate, ethiodized oil, gallium citrate, iocarmic acid, iocetamic acid, iodamide, iodipamide, iodoxamic acid, iogulamide, iohexol, iopamidol, iopanoic acid, ioprocemic acid, iosefamic acid, ioseric acid, iosulamide meglumine, iosemetic acid, iotasul, iotetric acid, iothalamic acid, iotroxic acid, ioxaglic acid, ioxotrizoic acid, ipodate, meglumine, metrizamide, metrizoate, propyliodone, thallous chloride or their combinations. The composition comprises one or more ultrasound contrast agents, where the ultrasound contrast agent includes a liposome or dextran. The liposome is gas-filled.

The method further involves performing an operative, intravascular, laparoscopic or endoscopic procedure. The method further involves administering an additional composition, which comprises a therapeutic agent, diagnostic agent or their mixtures. The additional composition comprises an immunoconjugate, which comprises one or more anti- CD74 binding molecules

conjugated to one or more lipids, polymeric carriers, micelles, nanoparticles or their combinations, and one more effectors. The anti-CD74 antibody or its fragment is conjugated to the therapeutic agent, diagnostic agent or their mixtures by chemical conjugation or genetic fusion. The additional composition comprises one or more drugs, prodrugs, toxins, enzymes, radioisotopes, immunomodulators, cytokines, hormones, antibodies, oligonucleotides or their combinations. The composition is administered before, during, simultaneously, or after the administration of the additional composition (all claimed).

ADVANTAGE - The immunoconjugate of (I) has a significant effect in evocation of a humoral and/or cellular immune response in a mammal.

DESCRIPTION OF DRAWINGS - The figure shows a graph representing the dose-response curves for 3',5'-O-dioleoyl-floxuridine.

L70 ANSWER 24 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-313738 [29] WPIX
CROSS REFERENCE: 2003-801085
DOC. NO. CPI: C2004-119121 [29]
DOC. NO. NON-CPI: N2004-249776 [29]
TITLE: Treating cancer and metabolic diseases by administering a multi-specific antibody having a targeting arm that binds to an antigen and a capture arm that binds to a polymer conjugate comprising a therapeutic agent
DERWENT CLASS: A96; B04; C06; D16; K08; S03
INVENTOR: GOLDENBERG D M; GRIFFITHS G L; HANSEN H J
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 1

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| US 20040043030 | A1 | 20040304 | (200429)* | EN | 24 | [0] |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| US 20040043030 | A1 Provisional | US 2001-308605P | 20010731 |
| US 20040043030 | A1 CIP of | US 2002-209592 | 20020731 |
| US 20040043030 | A1 | US 2003-456580 | 20030609 |

PRIORITY APPLN. INFO: US 2003-456580 20030609
US 2001-308605P 20010731
US 2002-209592 20020731

AB US 20040043030 A1 UPAB: 20050528

NOVELTY - Diagnosing or treating a disease or disorder, involves administering to a tissue a multi-specific antibody (I) or antibody fragment, comprising a targeting arm that binds to an antigen on the target site, and a capture arm that binds to a polymer conjugate, and administering to the tissue a polymer conjugate that binds to the capture arm, the polymer conjugate comprising a polymer conjugated to a diagnostic or therapeutic agent.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for photodynamic diagnosis or treatment of a disease or disorder or intravascular or endoscopic method for diagnosing or treating a disease or disorder, involves administering to a tissue a multi-specific antibody or antibody fragment, comprising a targeting arm that binds to an antigen on the target site, and a capture arm that binds to a polymer conjugate, and administering to the tissue a polymer conjugate that binds to the capture arm, the polymer

conjugate comprising a polymer conjugated to a diagnostic or therapeutic agent.

ACTIVITY - Cytostatic; Antiinflammatory; Nootropic; Neuroprotective; Antiatherosclerotic; Vasotropic; Thrombolytic; Immunosuppressive; Nephrotropic; Dermatological; Antirheumatic; Antiarthritic; Hemostatic; Analgesic; Antidiabetic; Antiulcer; Hepatotropic; Thyromimetic; Antiallergic; Antibacterial; Fungicide; Virucide; Antiparasitic; Protozoacide; Antianemic.

A subject who has colon cancer that expressed the CEA antigen was given a 100 mg/m2 dose of the bi-specific antibody hMN-14 x 374 F(ab')2 x Fab'. After 24 hours, the subject was then given an equimolar dose of the indium coupled of the AcLys (diethylenetriaminepentaacetic acid)Glu6(SN-38)6Lys(diethylenetriaminepentaacetic acid)NH2 diethylenetriaminepentaacetic acid-polymer-drug, conjugate. The diethylenetriaminepentaacetic acid-polymer-drug was localized selectively at the tumor due to the pretargeting with the multi-specific antibody, causing a high concentration of the active agent SN-38 to also be localized. Over time, free SN-38 was released from the localized conjugate, exerting a therapeutic effect on the tumors.

MECHANISM OF ACTION - Immunotherapy.

USE - The method is useful for diagnosing or treating a disease or disorder chosen from cancer (esophageal, gastric, colonic, rectal, pancreatic, lung, breast, ovarian, urinary bladder, endometrial, cervical, testicular, renal, adrenal and liver cancer, solid tumor, B- cell malignancy or T-cell malignancy); cardiovascular lesion; an inflammatory disease; neurodegenerative disease; metabolic disease; and an infectious disease. The B-cell malignancy is chosen from indolent forms of B-cell lymphomas, aggressive forms of B-cell lymphomas, chronic lymphatic leukemias, acute lymphatic leukemias, and multiple myeloma. The solid tumor is chosen melanoma, carcinoma (preferably renal carcinoma, lung carcinoma, intestinal carcinoma, and stomach carcinoma), glioma and sarcoma. The cardiovascular lesion is chosen from infarct, clot, embolus, atherosclerotic plaque and ischemia. The neurodegenerative disease is Alzheimer's disease. The metabolic disease is amyloidosis, where the antibody binds amyloid. The disease or disorder is displaced or ectopic normal tissue chosen from endometrium, thymus, spleen and parathyroid. The method can be used for normal tissue ablation, where the tissue is chosen from bone marrow and spleen. The disease or disorder is an autoimmune disease such as myasthenia gravis, lupus nephritis, lupus erythematosus, and rheumatoid arthritis, Class III autoimmune diseases such as immune-mediated thrombocytopenias, such as acute idiopathic thrombocytopenic purpura and chronic idiopathic thrombocytopenic purpura, dermatomyositis, Sjogren's syndrome, multiple sclerosis, Sydenham's chorea, myasthenia gravis, systemic lupus erythematosus, lupus nephritis, rheumatic fever, polyglandular syndromes, bullous pemphigoid, diabetes mellitus, Henoch-Schonlein purpura, post-streptococcal nephritis, erythema nodosum, Takayasu's arteritis, Addison's disease, rheumatoid arthritis, sarcoidosis, ulcerative colitis, erythema multiforme, IgA nephropathy, polyarteritis nodosa, ankylosing spondylitis, Goodpasture's syndrome, thromboangitis ubiterans, primary biliary cirrhosis, Hashimoto's thyroiditis, thyrotoxicosis, scleroderma, chronic active hepatitis, polymyositis/dermatomyositis, polychondritis, pemphigus vulgaris, Wegener's granulomatosis, membranous nephropathy, amyotrophic lateral sclerosis, tabes dorsalis, giant cell arteritis/polymyalgia, pernicious anemia, rapidly progressive glomerulonephritis, or fibrosing alveolitis. The infectious disease is chosen from bacterial, fungal, parasitic and viral lesion. The infectious disease is caused by a fungus chosen from Microsporum, Trichophyton, Epidermophyton, Sporothrix schenckii, Cyrptococcus neoformans, Coccidioides immitis, Histoplasma capsulatum, Blastomyces dermatitidis, and Candida albicans. The infectious disease is caused by a virus chosen from HIV, herpes virus, cytomegalovirus, rabies virus, influenza virus, hepatitis B virus, Sendai virus, feline leukemia virus, Reo virus, polio virus, human serum parvo-like virus, simian virus 40, respiratory syncytial virus, mouse mammary tumor virus, Varicella-Zoster virus, Dengue

virus, rubella virus, measles virus, adenovirus, human T-cell leukemia viruses, Epstein-Barr virus, murine leukemia virus, mumps virus, vesicular stomatitis virus, Sindbis virus, lymphocytic choriomeningitis virus, wart virus and blue tongue virus. The infectious disease is caused by a bacterium chosen from Bacillus anthracis, Streptococcus agalactiae, Legionella pneumophilia, Streptococcus pyogenes, Escherichia coli, Neisseria gonorrhoeae, Neisseria meningitidis, Pneumococcus, Hemophilus influenzae B, Treponema pallidum, Lyme disease spirochetes, Pseudomonas aeruginosa, Mycobacterium leprae, Brucella abortus, Mycobacterium tuberculosis, and Tetanus toxin. The infectious disease is caused by a protozoa chosen from Plasmodium falciparum, Plasmodium vivax, Toxoplasma gondii, Trypanosoma rangeli, Trypanosoma cruzi, Trypanosoma rhodesiensei, Trypanosoma brucei, Schistosoma mansoni, Schistosoma japanicum, Babesia bovis, Elmeria tenella, Onchocerca volvulus, Leishmania tropica, Trichinella spiralis, Onchocerca volvulus, Theileria parva, Taenia hydatigena, Taenia ovis, Taenia saginata, Echinococcus granulosus, and Mesocestoides corti. The infectious disease is caused by a mycoplasma chosen from Mycoplasma arthritidis, M. hyorhinis, M. orale, M. arginini, Acholeplasma laidlawii, M. salivarum and M. pneumoniae. The cancer is preferably chosen from carcinoembryonic antigen (CEA)-expressing tumor or a CD20-expressing malignancy. The CD20-expressing malignancy is a B-cell lymphoma or leukemia (claimed).

L70 ANSWER 25 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-767381 [72] WPIX
CROSS REFERENCE: 1999-045130; 2001-041267; 2001-122704; 2002-351262; 2005-010089
DOC. NO. CPI: C2003-210871 [72]
DOC. NO. NON-CPI: N2003-614702 [72]
TITLE: New humanized, human or chimeric anti-CD74 antibody or fragment, useful for diagnosing or treating a CD74 expressing malignancy, an immune dysregulation disease, an autoimmune disease or graft versus host disease
DERWENT CLASS: B04; D16; S03
INVENTOR: GOLDENBERG D M; HANSEN H; HANSEN H J; LEUNG S; QU Z
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC; (MCCA-I) MCCALL J D
COUNTRY COUNT: 101

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2003074567 | A2 | 20030912 | (200372)* | EN | 91[10] | |
| AU 2003215732 | A1 | 20030916 | (200430) | EN | | |
| US 20040115193 | A1 | 20040617 | (200440) | EN | | |
| EP 1483294 | A2 | 20041208 | (200480) | EN | | |
| KR 2004089695 | A | 20041021 | (200514) | KO | | |
| CN 1649902 | A | 20050803 | (200578) | ZH | | |
| JP 2006502699 | W | 20060126 | (200609) | JA | 56 | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2003074567 | A2 | WO 2003-GB890 | 20030303 |
| US 20040115193 | A1 Provisional | US 2002-360259P | 20020301 |
| AU 2003215732 | A1 | AU 2003-215732 | 20030303 |
| CN 1649902 | A | CN 2003-809863 | 20030303 |

| | |
|---|---|
| EP 1483294 A2 | EP 2003-743421 20030303 |
| US 20040115193 A1 | US 2003-377122 20030303 |
| EP 1483294 A2 | WO 2003-GB890 20030303 |
| CN 1649902 A | WO 2003-GB890 20030303 |
| KR 2004089695 A | KR 2004-713665 20040901 |
| JP 2006502699 W | JP 2003-573032 20030303 |
| JP 2006502699 W | WO 2003-GB890 20030303 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| AU 2003215732 A1 | Based on | WO 2003074567 A |
| EP 1483294 A2 | Based on | WO 2003074567 A |
| JP 2006502699 W | Based on | WO 2003074567 A |

PRIORITY APPLN. INFO: US 2002-360259P 20020301
US 2003-377122 20030303

AB WO 2003074567 A2 UPAB: 20060203

NOVELTY - A humanized, human or chimeric anti-CD74 antibody or fragment, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a humanized anti-CD74 monoclonal antibody (mAb) or its fragment comprising light and heavy chain variable regions having complementarity-determining regions (CDRs) of murine anti -CD74 (mLL1) and the framework (FR) regions of a human antibody, where the light chain variable region of the humanized mAb comprises CDRs of a light chain variable region of a murine anti-CD74 mAb, that comprises:

(a) CDR1 with amino acid sequence S1, (S1) RSSQSLVHRNGNTYLH;

(b) CDR2 comprising amino acid sequence S2, (S2) TVSNRFS;

(c) CDR3 comprising amino acid sequence S3, (S3) SQSSHVPPT; and

(d) where the heavy chain variable region of the humanized mAb comprises CDRs of a heavy chain variable region of the murine anti -CD74 mAb, that comprises CDR1 comprising amino acid sequence S4, (S4) NYGVN;

(e) CDR2 comprising amino acid sequence S5, (S5) WINPNTGEPTFDDDFKG; and

(f) CDR3 comprising amino acid sequence S6, (S6) SRGKNEAWFAY;

(2) a murine anti-CD74 mAb or fragment, comprising CDRs of a light chain variable region of a murine anti -CD74 mAb, that comprises CDR1 comprising amino acid sequence S1, CDR2 comprising amino acid sequence S2, and CDR3 comprising amino acid sequence S3, or CDRs of a heavy chain variable region of a murine anti-CD74 mAb, that comprises CDR1 comprising amino acid sequence S4, CDR2 comprising amino acid sequence S5, and CDR3 comprising amino acid sequence S6;

(3) an antibody fusion protein comprising four or more Fvs, or Fab's of the mAbs or fragments cited above, and/or one or more Fvs or Fab's from antibodies specific for a tumor cell marker that is not a CD74 antigen;

(4) an immunoconjugate conjugate, comprising an antibody component comprising at least one mAb or fragment or antibody fusion protein cited above, that binds to CD74, where the antibody component is linked to a diagnostic or therapeutic agent;

(5) treating a disease or disorder comprising administering to a subject a therapeutic composition comprising a pharmaceutically acceptable carrier and at least one mAb or fragment or antibody fusion protein or an immunoconjugate cited above;

(6) treating a malignancy, comprising administering to a subject with a CD74 antigen positive malignancy other than lymphoma or leukemia, a therapeutic composition comprising a carrier and at least one mAb or fragment or an antibody fusion protein cited above;

(7) treating a subject with at least one disease diagnosed as an immune dysregulation disease and autoimmune disease, comprising administering to the subject a therapeutic composition comprising a carrier and at least one mAb or fragment or an antibody fusion protein cited above;

(8) treating or diagnosing one of the diseases selected from the group consisting of lymphoma, leukemia, other CD-74 expressing malignancies, immune dysregulation disease, autoimmune disease and their combination, comprising administering a therapeutic composition comprising a carrier and at least one mAb or fragment or an antibody fusion protein cited above, where at least one therapeutic agent is linked to the mAb or fragment or the Fvs or Fab's of the antibody fusion protein by chemical conjugation or by genetic fusion;

(9) a vaccine comprising covalent linked of mAbs or fragments cited above to class-I or class-II MHC antigenic peptides forming an antibody conjugate, where the vaccine is used to treat patients with cancer or infectious disease;

(10) a bispecific or multispecific antibody, where the mAbs or fragments or antibody fusion proteins cited above, are linked to an antibody or antibody fragment specific for a cancer or inflammatory cell marker substance, an epitope on the surface of a infectious disease organism, or a noxious substance in the blood or other body fluid;

(11) a DNA sequence comprising a nucleic acid encoding a mAb or fragment selected from:

(a) an anti-CD74mAb or fragment cited above;

(b) an immunoconjugate of (4);

(c) an antibody fusion protein or fragment comprising at least two of the anti-CD74 mAbs or fragments cited above;

(d) an antibody fusion protein or fragment of (3);

(e) a vaccine of (9); and

(f) a bispecific or multispecific antibody of (10);

(12) an expression vector comprising the DNA sequence of (11);

(13) a host cell comprising the DNA sequence of (11); and

(14) expression of an anti-CD74mAb or fragment or antibody fusion protein or fragment, comprising transfecting a host cell with a DNA sequence of (11), and culturing the cell secreting the anti-CD74 mAb or antibody fusion protein or their fragments.

ACTIVITY - Cytostatic; Immunosuppressive; Immunomodulator.

No biological data given.

MECHANISM OF ACTION - CD74-Antagonist.

USE - The naked anti-CD74 antibody or a naked antibody fusion protein or fragment, or a therapeutic or diagnostic conjugate comprising an anti-CD74 antibody is useful for diagnosing or treating a disorder or a disease that is a CD74 expressing malignancy (solid tumor, non-Hodgkin's lymphoma, Hodgkin's lymphoma, multiple myeloma, another B-cell malignancy and a T-cell malignancy), an immune dysregulation disease, an autoimmune disease, organ graft rejection, and graft versus host disease. The solid tumor is melanoma, carcinoma and sarcoma. The carcinoma is a renal carcinoma, lung carcinoma, intestinal carcinoma, stomach carcinoma and melanoma. The B-cell malignancy is of non-Hodgkin's lymphoma, Hodgkin's lymphoma, indolent forms of B-cell lymphomas, aggressive forms of B-cell lymphomas, chronic lymphatic leukemias, acute lymphatic leukemias, and multiple myeloma (all claimed).

L70 ANSWER 26 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-697522 [66] WPIX
DOC. NO. CPI: C2003-191816 [66]
DOC. NO. NON-CPI: N2003-556970 [66]
TITLE: New humanized anti-CD20 monoclonal antibody (MAb) that retains substantially the B -cell and B-cell lymphoma and leukemia cell targeting of the murine anti-

CD20 MAb, useful for treating B-cell lymphoma, leukemia or an autoimmune diseases

DERWENT CLASS: B04; D16; K08; S03
INVENTOR: GOLDENBERG D M; HANSEN H; QU Z
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC; (MCCA-I) MCCALL J D
COUNTRY COUNT: 101

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2003068821 | A2 | 20030821 | (200366)* | EN | 106[12] | |
| US 20030219433 | A1 | 20031127 | (200378) | EN | | |
| AU 2003208415 | A1 | 20030904 | (200428) | EN | | |
| KR 2004086383 | A | 20041008 | (200512) | KO | | |
| EP 1519959 | A2 | 20050406 | (200523) | EN | | |
| JP 2006500904 | W | 20060112 | (200604) | JA | 71 | |
| CN 1662557 | A | 20050831 | (200607) | ZH | | |
| IN 2004002017 | P4 | 20060224 | (200619) | EN | | |
| US 7151164 | B2 | 20061219 | (200702) | EN | | |
| US 20070020259 | A1 | 20070125 | (200710) | EN | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2003068821 | A2 | WO 2003-GB665 | 20030214 |
| US 20030219433 | A1 Provisional | US 2002-356132P | 20020214 |
| US 7151164 | B2 Provisional | US 2002-356132P | 20020214 |
| US 20030219433 | A1 Provisional | US 2002-416232P | 20021007 |
| US 7151164 | B2 Provisional | US 2002-416232P | 20021007 |
| IN 2004002017 | P4 | WO 2003-GB665 | |
| AU 2003208415 | A1 | AU 2003-208415 | 20030214 |
| CN 1662557 | A | CN 2003-808357 | 20030214 |
| EP 1519959 | A2 | EP 2003-706703 | 20030214 |
| JP 2006500904 | W | JP 2003-567947 | 20030214 |
| US 20030219433 | A1 | US 2003-366709 | 20030214 |
| US 7151164 | B2 | US 2003-366709 | 20030214 |
| EP 1519959 | A2 | WO 2003-GB665 | 20030214 |
| JP 2006500904 | W | WO 2003-GB665 | 20030214 |
| KR 2004086383 | A | KR 2004-712676 | 20040814 |
| IN 2004002017 | P4 | IN 2004-CN2017 | 20040909 |
| US 20070020259 | A1 Provisional | US 2002-356132P | 20020214 |
| US 20070020259 | A1 Provisional | US 2002-416232P | 20021007 |
| US 20070020259 | A1 Cont of | US 2003-366709 | 20030214 |
| US 20070020259 | A1 | US 2006-534103 | 20060921 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| AU 2003208415 | A1 Based on | WO 2003068821 A |
| EP 1519959 | A2 Based on | WO 2003068821 A |
| JP 2006500904 | W Based on | WO 2003068821 A |

PRIORITY APPLN. INFO: US 2002-416232P 20021007
US 2002-356132P 20020214
US 2003-366709 20030214
US 2006-534103 20060921

AB WO 2003068821 A2 UPAB: 20060120

NOVELTY - A humanized anti-CD20 (hCD20) monoclonal antibody (MAb) or its antigen-binding fragment comprising the complementarity determining regions (CDRs) of at least one murine anti-CD20 MAb variable region and the framework regions (FRs) of at least one human IVlAb variable region, where humanized anti-CD20 MAb or its fragment retains substantially the B-cell and B-cell lymphoma and leukemia cell targeting of the murine anti-CD20 MAb, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(1) a humanized antibody or its fragment comprising the hA20Vk and hA2VH1 or hA2VH2;

(2) a chimeric anti-CD20 (cCD20) monoclonal antibody, (MAb) or its fragment comprising the CDRs of at least one murine anti-CD20 MAb variable region and the FRs of at least one murine anti-CD 20 MAb variable region;

(3) a human anti-CD20 (huD20)MAb;

(4) an antibody fusion protein or its fragment comprising at least two MAbs or their fragments, selected from the anti-CD20 MAbs cited above;

(5) a DNA sequence comprising a nucleic acid encoding a MAb or its fragment selected from the anti-CD20 MAb or their fragments and the antibody fusion protein cited above;

(6) an expression vector comprising the DNA sequence;

(7) a host cell comprising the DNA sequence or the expression vector;

(8) a method for expressing an anti-CD20 MAB, antibody fusion protein or their fragment;

(9) a B-lymphoma and leukemia cell targeting diagnostic or therapeutic conjugate comprising an antibody component comprising the anti-CD20 MAb, antibody fusion protein or their fragment that binds to the cell, where the antibody component is bound to at least one diagnostic or at least one therapeutic agent;

(10) a method for treating or diagnosing a B-cell lymphoma or leukemia or an autoimmune disease in a subject; and

(11) a method for pretargeting a cell in a patient suffering from a B-cell lymphoma or leukemia or an autoimmune disease.

ACTIVITY - Cytostatic; Immunomodulator; Dermatological; Antiinflammatory; Antiarthritic. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The antibodies, fusion proteins and conjugates are useful for diagnosing or preventing B- cell lymphoma, leukemia or an autoimmune disease (claimed), e.g. thrombocytopenia, lupus or rheumatoid arthritis.

L70 ANSWER 27 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-351262 [38] WPIX
CROSS REFERENCE: 1999-045130; 2001-041267; 2001-122704; 2003-767381; 2005-010089
DOC. NO. CPI: C2002-099668 [38]
TITLE: Treating B-cell, T-cell, myeloid cell, mast cell or plasma cell disorders such as malignancy, involves administering an antibody
DERWENT CLASS: B04; C06; D16
INVENTOR: GOLDENBERG D M
PATENT ASSIGNEE: (GOLD-I) GOLDENBERG D M
COUNTRY COUNT: 1

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| US 20020041847 | A1 | 20020411 | (200238)* | EN | 17 | [0] |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| US 20020041847 | A1 CIP of | US 1998-38995 | 19980312 |
| US 20020041847 | A1 CIP of | US 1999-307816 | 19990510 |
| US 20020041847 | A1 | US 2001-921290 | 20010803 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| US 20020041847 | A1 | CIP of | US 6134982 A |
| US 20020041847 | A1 | CIP of | US 6306393 B |

PRIORITY APPLN. INFO: US 2001-921290 20010803
US 1998-38995 19980312
US 1999-307816 19990510

AB US 20020041847 A1 UPAB: 20050525

NOVELTY - Treating a B-cell, T-cell, myeloid cell, mast cell, or plasma cell disorder in a domestic animal, comprising administering an antibody specific for an antigen or epitope on one of the cells, is new.

ACTIVITY - Immunosuppressive; Cytostatic.

A 65 pound, 7 year old male golden retriever diagnosed with diffuse large cell aggressive lymphomase was placed on a combination chemotherapy with vincristine, cyclophosphamide, prednisolone, and doxorubicin, with good response. The dog was subsequently characterized with progressive lymphadenopathy, and seven months later found to have extensive lymphoma infiltration of bone marrow, extensive lymphoadenopathy of neck, chest abdomen and pelvis, and hepatosplenomegaly. The dog was given therapy with 120 mg 1F5 monoclonal antibody, intravenously, by infusion. The treatment was repeated weekly for 4 weeks. Four months after the final dose, a computerized tomography scan of the dog shows no signs of lymphoma.

MECHANISM OF ACTION - None given.

USE - For treating B-cell, T-cell, myeloid cell, mast cell, or plasma cell disorders, particularly a malignancy, or autoimmune disorder, in a domestic animal, such as a dog, cat or horse (claimed).

L70 ANSWER 28 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-041267 [05] WPIX
CROSS REFERENCE: 1999-045130; 2001-122704; 2002-351262; 2003-767381; 2005-010089
DOC. NO. CPI: C2001-012032; C2006-096464; C2006-101877; C2006-101878 [05] [31] [33] [33]
TITLE: New composition, useful for treating autoimmune disease e.g. rheumatoid arthritis, comprising antibody directed against B cell antigen CD22
DERWENT CLASS: B04; D16
INVENTOR: GOLDENBERG D M; HANSEN H J
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 92

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2000074718 | A1 | 20001214 | (200105)* | EN | 39 | [0] |
| AU 2000056005 | A | 20001228 | (200119) | EN | | |
| EP 1194167 | A1 | 20020410 | (200232) | EN | | |
| KR 2002020730 | A | 20020315 | (200263) | KO | | |
| JP 2003501401 | W | 20030114 | (200306) | JA | 44 | |

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|---|---|---|---|---|
| US 20030133930 | A1 | 20030717 (200348) | EN | |
| EP 1543839 | A1 | 20050622 (200541) | EN | |
| AU 782160 | B2 | 20050707 (200551) | EN | |
| US 20050191300 | A1 | 20050901 (200558) | EN | |
| US 20060051349 | A1 | 20060309 (200618) | EN | |
| AU 2005220209 | A1 | 20051103 (200631)# | EN | 34[0] |
| AU 2005220211 | A1 | 20051103 (200633)# | EN | 34[0] |
| AU 2005220212 | A1 | 20051103 (200633)# | EN | 34[0] |
| US 7074403 | B1 | 20060711 (200646) | EN | |
| US 20070020265 | A1 | 20070125 (200710) | EN | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2000074718 | A1 | WO 2000-US15780 | 20000609 |
| US 20030133930 | A1 Provisional | US 1999-138284P | 19990609 |
| US 20050191300 | A1 Provisional | US 1999-138284P | 19990609 |
| US 20060051349 | A1 Provisional | US 1999-138284P | 19990609 |
| US 7074403 | B1 Provisional | US 1999-138284P | 19990609 |
| AU 2000056005 | A | AU 2000-56005 | 20000609 |
| AU 782160 | B2 | AU 2000-56005 | 20000609 |
| EP 1194167 | A1 | EP 2000-941278 | 20000609 |
| EP 1543839 | A1 Div Ex | EP 2000-941278 | 20000609 |
| US 20030133930 | A1 Cont of | US 2000-590284 | 20000609 |
| US 20050191300 | A1 Cont of | US 2000-590284 | 20000609 |
| US 20060051349 | A1 Div Ex | US 2000-590284 | 20000609 |
| US 7074403 | B1 | US 2000-590284 | 20000609 |
| EP 1194167 | A1 | WO 2000-US15780 | 20000609 |
| JP 2003501401 | W | WO 2000-US15780 | 20000609 |
| JP 2003501401 | W | JP 2001-501252 | 20000609 |
| KR 2002020730 | A | KR 2001-715884 | 20011210 |
| US 20030133930 | A1 | US 2003-350096 | 20030124 |
| EP 1543839 | A1 | EP 2005-75555 | 20000609 |
| US 20050191300 | A1 | US 2005-104594 | 20050413 |
| US 20060051349 | A1 | US 2005-222838 | 20050912 |
| AU 2005220209 | A1 | AU 2005-220209 | 20051006 |
| AU 2005220211 | A1 | AU 2005-220211 | 20051006 |
| AU 2005220212 | A1 | AU 2005-220212 | 20051006 |
| US 20070020265 | A1 Provisional | US 1999-138284P | 19990609 |
| US 20070020265 | A1 Cont of | US 2000-590284 | 20000609 |
| US 20070020265 | A1 Div Ex | US 2005-104594 | 20050413 |
| US 20070020265 | A1 | US 2006-534124 | 20060921 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO | |
|---|---|---|---|---|
| AU 782160 | B2 | Previous Publ | AU 2000056005 | A |
| AU 2005220209 | A1 | Div ex | AU 782160 | B |
| AU 2005220211 | A1 | Div ex | AU 782160 | B |
| AU 2005220212 | A1 | Div ex | AU 782160 | B |
| EP 1543839 | A1 | Div ex | EP 1194167 | A |
| AU 2000056005 | A | Based on | WO 2000074718 | A |
| EP 1194167 | A1 | Based on | WO 2000074718 | A |
| JP 2003501401 | W | Based on | WO 2000074718 | A |
| AU 782160 | B2 | Based on | WO 2000074718 | A |
| US 20070020265 | A1 | Cont of | US 7074403 | B |

PRIORITY APPLN. INFO: US 1999-138284P 19990609

| | |
|---|---|
| US 2000-590284 | 20000609 |
| US 2003-350096 | 20030124 |
| US 2005-104594 | 20050413 |
| US 2005-222838 | 20050912 |
| AU 2005-220209 | 20051006 |
| AU 2005-220211 | 20051006 |
| AU 2005-220212 | 20051006 |
| US 2006-534124 | 20060921 |

AB WO 2000074718 A1 UPAB: 20060116

NOVELTY - Treating an autoimmune disorder, comprising administering a therapeutic composition (A) comprising a carrier and at least one antibody (Ab) to a B cell antigen (Ag), is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for (A).

ACTIVITY - Antiinflammatory; antidiabetic; antianemic; immunomodulatory; antithyroid; thyromimetic; immunosuppressive; nephrotropic; neuroprotective; hepatotropic; virucide; antiulcer; antiarthritic; antirheumatic; dermatological; antipyretic.

MECHANISM OF ACTION - Suppression of B cells.

USE - The method, optionally in combination with other treatments, is used to treat a wide range of autoimmune disorders, particularly of Class III. Autoimmune diseases include various forms of purpura, myasthenia gravis, diabetes mellitus, rheumatoid arthritis, Sjogren's syndrome, amyotrophic lateral sclerosis, pernicious anemia, dermatomyositis, Sydenham's chorea, myasthenia gravis, systemic lupus erythematosus, lupus nephritis, rheumatic fever, polyglandualr syndromes, bullous pemphigoid, Henoch-Schonlein purpura, post-streptococcal nephritis, erythema nodosum, Takayasu's arteritis, Addison's disease, multiple sclerosis, sarcoiditis, ulcerative colitis, erythema multiforme, IgA nephropathy, polyarteritis nodosa, Goodpasture's syndrome, thromboangitis, primary biliary cirrhosis, Hashimoto's throiditis, thyrotoxicosis, scleroderma, chronic active hepatitis, polymyositis/dermatomyositis, pamphigus vulgaris, Wegener's granulomatosis, membranous nephropathy, amyotrophic lateral sclerosis, tabes dorsalis, giant cell arteritis/polymyalgia, rapidly progressive glomerulonephritis and fibrosing alveolitis. The ability of humanized LL2 antibody to treat rheumatoid arthritis was tested in a 60 year old male with severe progressive rheumatoid arthritis of the finger joints, wrists and elbows. 600 mg hLL2 was administered intravenously each week for 8 weeks. After 3 weeks, a 30% improvement is observed which is maintained for 6 months. The patient is treated again with hLL2 at the same dose and frequency. 6 months after therapy, a 70% improvement is observed. No human anti-hLL2 antibodies were observed at any time during or after the hLL2 therapy. Though normal B-cells were reduced, no other side effects were seen.

ADVANTAGE - Relatively small doses of (A) are required and the method may reduce the required amount (and thus associated side effects) of other therapeutic agents such as cytotoxins or corticosteroids.

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| L70 ANSWER 29 OF 46 | WPIX COPYRIGHT 2007 THE THOMSON CORP on STN |
| ACCESSION NUMBER: | 2001-122704 [13] WPIX |
| CROSS REFERENCE: | 1999-045130; 2001-041267; 2002-351262; 2003-767381; 2005-010089 |
| DOC. NO. CPI: | C2001-035504 [13] |
| TITLE: | Treating B-cell malignancies e.g. indolent and aggressive B-cell lymphomas and chronic and acute lymphatic leukemias comprises administrating compositions containing a carrier and naked anti-CD22 antibodies |
| DERWENT CLASS: | B04; B05; D16; K08 |
| INVENTOR: | GOLDENBERG D M |
| PATENT ASSIGNEE: | (IMMU-N) IMMUNOMEDICS INC |

COUNTRY COUNT:. 91

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 2000067795 | A1 | 20001116 | (200113)* | EN | 52[0] | |
| AU 2000048296 | A | 20001121 | (200113) | EN | | |
| EP 1178826 | A1 | 20020213 | (200219) | EN | | |
| JP 2002544173 | W | 20021224 | (200313) | JA | 52 | |
| AU 774044 | B2 | 20040617 | (200467) | EN | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2000067795 | A1 | WO 2000-US12583 | 20000510 |
| AU 2000048296 | A | AU 2000-48296 | 20000510 |
| AU 774044 | B2 | AU 2000-48296 | 20000510 |
| EP 1178826 | A1 | EP 2000-930484 | 20000510 |
| JP 2002544173 | W | JP 2000-616820 | 20000510 |
| EP 1178826 | A1 | WO 2000-US12583 | 20000510 |
| JP 2002544173 | W | WO 2000-US12583 | 20000510 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| AU 774044 | B2 | Previous Publ | AU 2000048296 A |
| AU 2000048296 | A | Based on | WO 2000067795 A |
| EP 1178826 | A1 | Based on | WO 2000067795 A |
| JP 2002544173 | W | Based on | WO 2000067795 A |
| AU 774044 | B2 | Based on | WO 2000067795 A |

PRIORITY APPLN. INFO: US 1999-307816 19990510

AB WO 2000067795 A1 UPAB: 20050524

NOVELTY - Treating a B-cell malignancy comprises administering a therapeutic composition comprising at least one naked anti-CD19 antibody.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for kits for human therapeutic use for treating B-cell malignancies.

ACTIVITY - Cytostatic. A patient with diffuse large-cell aggressive lymphoma showed minimal response on COP. After 7 months, they showed good response to CDA therapy, however, 15 months later, they had progressive lymphadenopathy and, 7 months later than this, showed extensive lymphoma infiltration of bone marrow, extensive lymphadenopathy of the neck, chest, abdomen and pelvis, and hepatosplenomegaly (day 0). The patient received humanized LL2 antibody (634 milligrams) by intravenous infusion, which was repeated 6, 13 and 20 days after the initial treatment. Immediately following the last dose, the serum value of hLL2 was 389.7 micrograms/milliliter and 1 month after the last dose the serum value was 186.5 micrograms/milliliter. Five months after the final dose of hLL2, the computerized tomography showed no evidence of lymphoma, resolution of splenomegaly and no liver abnormality, and subsequent histology revealed no evidence of lymphoma in the bone marrow. Normal B- cells in the blood prior to therapy with hLL2 were completed depleted from the blood 2 months post-therapy and there was minimal reappearance of normal B cells five months post-therapy.

MECHANISM OF ACTION - None given.

USE - The method is used to treat B-cell malignancies including indolent and aggressive forms of B- cell lymphomas, chronic lymphatic leukemia, acute lymphatic leukemia and non-Hodgkin's lymphoma (claimed). It

may also be used to prevent, mitigate or reverse radiation- or drug-induced toxicity of normal cells, particularly hematopoietic cells.

ADVANTAGE - The method uses comparatively low doses of anti-CD22 and/or anti-CD19 antibodies, which may be supplemented by therapeutic proteins or chemotherapeutic regimens.

L70 ANSWER 30 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-059667 [05] WPIX
CROSS REFERENCE: 1998-251058
DOC. NO. CPI: C1999-017504 [05]
TITLE: New selective cytotoxic reagent comprising onc protein coupled to antibody - is reactive with a cell surface marker, used particularly for killing malignant B or other tumour cells
DERWENT CLASS: B04; D16
INVENTOR: GOLDENBERG D M; NEWTON D L; RYBAK S M; GOLDENBERG M; NEWTON L; RYBAK M
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC; (USSH-C) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 81

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 9850435 | A1 | 19981112 | (199905)* | EN | 53 | [9] |
| AU 9872803 | A | 19981127 | (199915) | EN | | |
| EP 975674 | A1 | 20000202 | (200011) | EN | | |
| JP 2001507944 | W | 20010619 | (200140) | JA | 57 | |
| AU 745823 | B | 20020411 | (200237) | EN | | |
| US 6395276 | B1 | 20020528 | (200243) | EN | | |
| US 20020187153 | A1 | 20021212 | (200301) | EN | | |
| US 20030114368 | A1 | 20030619 | (200341) | EN | | |
| US 6653104 | B2 | 20031125 | (200378) | EN | | |
| JP 2004115529 | A | 20040415 | (200426) | JA | 32 | |
| EP 975674 | B1 | 20050817 | (200555) | EN | | |
| DE 69831224 | E | 20050922 | (200564) | DE | | |
| US 20050249738 | A1 | 20051110 | (200574) | EN | | |
| DE 69831224 | T2 | 20060323 | (200622) | DE | | |
| ES 2248898 | T3 | 20060316 | (200622) | ES | | |
| JP 3835827 | B2 | 20061018 | (200669) | JA | 25 | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 9850435 | A1 | WO 1998-US8983 | 19980501 |
| US 20020187153 | A1 Provisional | US 1996-28430P | 19961017 |
| US 6653104 | B2 Provisional | US 1996-28430P | 19961017 |
| US 6395276 | B1 Provisional | US 1997-46895P | 19970502 |
| US 20020187153 | A1 Provisional | US 1997-46895P | 19970502 |
| US 20030114368 | A1 Provisional | US 1997-46895P | 19970502 |
| US 20050249738 | A1 Provisional | US 1997-46895P | 19970502 |
| US 6653104 | B2 Provisional | US 1997-46895P | 19970505 |
| US 20020187153 | A1 CIP of | US 1997-949758 | 19971014 |
| US 6653104 | B2 CIP of | US 1997-949758 | 19971014 |
| AU 9872803 | A | AU 1998-72803 | 19980501 |
| AU 745823 | B | AU 1998-72803 | 19980501 |
| DE 69831224 | E | DE 1998-631224 | 19980501 |

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|---|---|
| DE 69831224 T2 | DE 1998-631224 19980501 |
| EP 975674 A1 | EP 1998-920171 19980501 |
| EP 975674 B1 | EP 1998-920171 19980501 |
| DE 69831224 E | EP 1998-920171 19980501 |
| ES 2248898 T3 | EP 1998-920171 19980501 |
| DE 69831224 T2 | EP 1998-920171 19980501 |
| JP 2001507944 W | JP 1998-548301 19980501 |
| JP 2004115529 A Div Ex | JP 1998-548301 19980501 |
| US 6395276 B1 | US 1998-71672 19980501 |
| US 20020187153 A1 CIP of | US 1998-71672 19980501 |
| US 20030114368 A1 Div Ex | US 1998-71672 19980501 |
| US 6653104 B2 CIP of | US 1998-71672 19980501 |
| US 20050249738 A1 Div Ex | US 1998-71672 19980501 |
| EP 975674 A1 | WO 1998-US8983 19980501 |
| JP 2001507944 W | WO 1998-US8983 19980501 |
| EP 975674 B1 | WO 1998-US8983 19980501 |
| DE 69831224 E | WO 1998-US8983 19980501 |
| DE 69831224 T2 | WO 1998-US8983 19980501 |
| US 20030114368 A1 | US 2001-918887 20010730 |
| US 20050249738 A1 Cont of | US 2001-918887 20010730 |
| US 20020187153 A1 | US 2001-986119 20011107 |
| US 6653104 B2 | US 2001-986119 20011107 |
| JP 2004115529 A | JP 2003-362606 20031022 |
| US 20050249738 A1 | US 2005-179844 20050711 |
| JP 3835827 B2 | JP 1998-548301 19980501 |
| JP 3835827 B2 | WO 1998-US8983 19980501 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO | |
|---|---|---|---|---|
| AU 745823 | B | Previous Publ | AU 9872803 | A |
| DE 69831224 | E | Based on | EP 975674 | A |
| ES 2248898 | T3 | Based on | EP 975674 | A |
| DE 69831224 | T2 | Based on | EP 975674 | A |
| US 20020187153 | A1 | CIP of | US 6083477 | A |
| US 6653104 | B2 | CIP of | US 6083477 | A |
| US 20020187153 | A1 | CIP of | US 6395276 | B |
| US 6653104 | B2 | CIP of | US 6395276 | B |
| US 20050249738 | A1 | Div ex | US 6395276 | B |
| AU 9872803 | A | Based on | WO 9850435 | A |
| EP 975674 | A1 | Based on | WO 9850435 | A |
| JP 2001507944 | W | Based on | WO 9850435 | A |
| AU 745823 | B | Based on | WO 9850435 | A |
| EP 975674 | B1 | Based on | WO 9850435 | A |
| DE 69831224 | E | Based on | WO 9850435 | A |
| DE 69831224 | T2 | Based on | WO 9850435 | A |
| JP 3835827 | B2 | Previous Publ | JP 2001507944 | W |
| JP 3835827 | B2 | Based on | WO 9850435 | A |

PRIORITY APPLN. INFO: US 1997-46895P 19970502
US 1996-28430P 19961017
US 1997-46895P 19970505
US 1997-949758 19971014
US 1998-71672 19980501
US 2001-918887 20010730
US 2001-986119 20011107
US 2005-179844 20050711

AB WO 1998050435 A1 UPAB: 20060201

New selective cytotoxic reagent (A) contains an onc protein (I) with ribonucleolytic activity joined to an antibody (Ab) specific for a surface marker expressed on B cells. Also new is nucleic acid (II) encoding (A).

USE - (A) are used to kill malignant B cells (lymphoma or leukaemia) or other malignant cells (neuroblastoma, melanoma or myeloma) that express the CD74 marker.

ADVANTAGE - (A) are up to 2000 times more active against malignant B cells than the human RNase counterpart or (I) itself; have greatly reduced side-effects (low systemic toxicity) and have minimal immunogenicity. Expression of (A) as a recombinant fusion protein avoids problems of heterogeneity associated with chemically produced conjugates.

L70 ANSWER 31 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-045130 [04] WPIX
CROSS REFERENCE: 2001-041267; 2001-122704; 2002-351262; 2003-767381; 2005-010089
DOC. NO. CPI: C1999-014039 [04]
TITLE: Use of naked anti-CD22 antibody - for treating a B-cell malignancy, e.g. B-cell lymphomas, chronic lymphatic leukaemias or acute lymphatic leukaemias
DERWENT CLASS: B04; D16; K08; P34
INVENTOR: GOLDENBERG D M; GOLDENBERG M
PATENT ASSIGNEE: (GOLD-I) GOLDENBERG D M; (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 81

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 9842378 | A1 | 19981001 | (199904)* | EN | 40 | [0] |
| AU 9867610 | A | 19981020 | (199909) | EN | | |
| ZA 9802438 | A | 19990127 | (199910) | EN | 39 | |
| EP 969866 | A1 | 20000112 | (200008) | EN | | |
| AU 728325 | B | 20010104 | (200107) | EN | | |
| US 6183744 | B1 | 20010206 | (200109) | EN | | |
| US 6306393 | B1 | 20011023 | (200165) | EN | | |
| JP 2001518930 | W | 20011016 | (200176) | JA | 36 | |
| US 20020071807 | A1 | 20020613 | (200243) | EN | | |
| US 20030124058 | A1 | 20030703 | (200345) | EN | | |
| EP 1431311 | A1 | 20040623 | (200441) | EN | | |
| EP 1459768 | A2 | 20040922 | (200462) | EN | | |
| EP 969866 | B1 | 20050615 | (200540) | EN | | |
| DE 69830570 | E | 20050721 | (200548) | DE | | |
| ES 2241129 | T3 | 20051016 | (200571) | ES | | |
| DE 69830570 | T2 | 20051103 | (200572) | DE | | |
| US 20060057136 | A1 | 20060316 | (200620) | EN | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 9842378 | A1 | WO 1998-US5075 | 19980317 |
| US 6183744 | B1 Provisional | US 1997-41506P | 19970324 |
| US 6306393 | B1 Provisional | US 1997-41506P | 19970324 |
| US 20020071807 | A1 Provisional | US 1997-41506P | 19970324 |
| US 20030124058 | A1 Provisional | US 1997-41506P | 19970324 |
| US 6183744 | B1 | US 1998-38955 | 19980312 |
| US 6306393 | B1 CIP of | US 1998-38995 | 19980312 |

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|---|---|
| US 20020071807 A1 CIP of | US 1998-38995 19980312 |
| US 20030124058 A1 CIP of | US 1998-38995 19980312 |
| AU 9867610 A | AU 1998-67610 19980317 |
| AU 728325 B | AU 1998-67610 19980317 |
| DE 69830570 E | DE 1998-630570 19980317 |
| DE 69830570 T2 | DE 1998-630570 19980317 |
| EP 969866 A1 | EP 1998-912936 19980317 |
| EP 1431311 A1 Div Ex | EP 1998-912936 19980317 |
| EP 1459768 A2 Div Ex | EP 1998-912936 19980317 |
| EP 969866 B1 | EP 1998-912936 19980317 |
| DE 69830570 E | EP 1998-912936 19980317 |
| ES 2241129 T3 | EP 1998-912936 19980317 |
| DE 69830570 T2 | EP 1998-912936 19980317 |
| JP 2001518930 W | JP 1998-545761 19980317 |
| EP 969866 A1 | WO 1998-US5075 19980317 |
| JP 2001518930 W | WO 1998-US5075 19980317 |
| EP 969866 B1 | WO 1998-US5075 19980317 |
| DE 69830570 E | WO 1998-US5075 19980317 |
| DE 69830570 T2 | WO 1998-US5075 19980317 |
| ZA 9802438 A | ZA 1998-2438 19980323 |
| US 6306393 B1 | US 1999-307816 19990510 |
| US 20020071807 A1 Cont of | US 1999-307816 19990510 |
| US 20030124058 A1 Cont of | US 1999-307816 19990510 |
| US 20020071807 A1 | US 2001-965796 20011001 |
| US 20030124058 A1 Cont of | US 2001-965796 20011001 |
| US 20030124058 A1 | US 2002-314330 20021209 |
| EP 1459768 A2 | EP 2004-75774 19980317 |
| EP 1431311 A1 | EP 2004-75775 19980317 |
| EP 969866 B1 Related to | EP 2004-75774 20040310 |
| EP 969866 B1 Related to | EP 2004-75775 20040310 |
| US 20060057136 A1 Provisional | US 1997-41506P 19970324 |
| US 20060057136 A1 CIP of | US 1998-38995 19980312 |
| US 20060057136 A1 Cont of | US 1999-307816 19990510 |
| US 20060057136 A1 Div Ex | US 2001-965796 20011001 |
| US 20060057136 A1 | US 2005-254754 20051021 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO | |
|---|---|---|---|---|
| AU 728325 | B | Previous Publ | AU 9867610 | A |
| EP 969866 | B1 | Related to | EP 1431311 | A |
| EP 969866 | B1 | Related to | EP 1459768 | A |
| EP 1431311 | A1 | Div ex | EP 969866 | A |
| EP 1459768 | A2 | Div ex | EP 969866 | A |
| DE 69830570 | E | Based on | EP 969866 | A |
| ES 2241129 | T3 | Based on | EP 969866 | A |
| DE 69830570 | T2 | Based on | EP 969866 | A |
| US 20030124058 | A1 | CIP of | US 6134982 | A |
| US 6306393 | B1 | CIP of | US 6183744 | A |
| US 20030124058 | A1 | Cont of | US 6306393 | B |
| AU 9867610 | A | Based on | WO 9842378 | A |
| EP 969866 | A1 | Based on | WO 9842378 | A |
| AU 728325 | B | Based on | WO 9842378 | A |
| JP 2001518930 | W | Based on | WO 9842378 | A |
| EP 969866 | B1 | Based on | WO 9842378 | A |
| DE 69830570 | E | Based on | WO 9842378 | A |
| DE 69830570 | T2 | Based on | WO 9842378 | A |
| US 20060057136 | A1 | CIP of | US 6134982 | A |
| US 20060057136 | A1 | Cont of | US 6306393 | B |

PRIORITY APPLN. INFO: US 1997-41506P 19970324
US 1998-38955 19980312
US 1998-38995 19980312
US 1999-307816 19990510
US 2001-965796 20011001
US 2002-314330 20021209
US 2005-254754 20051021

AB WO 1998042378 A1 UPAB: 20060114
Treatment of a B-cell malignancy comprises administering a composition comprising a carrier and at least one naked anti-CD22 antibody. Also claimed is the use of at least one naked anti-CD22 antibody in the preparation of the composition for use in the method above.
USE - The method can be used for treating indolent forms of B-cell lymphomas, aggressive forms of B- cell lymphomas, chronic lymphatic leukaemias, and acute lymphatic leukaemias (claimed).

L70 ANSWER 32 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1998-251058 [22] WPIX
CROSS REFERENCE: 1999-059667
DOC. NO. CPI: C1998-078255 [22]
TITLE: New conjugate of non-immunogenic toxin and cell-specific cytokine - and bi:specific antibody that binds cell marker and cytokine, used together for selective delivery of toxin to leukaemia and lymphoma cells
DERWENT CLASS: B04; D16; P34
INVENTOR: GOLDENBERG D M
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 78

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 9816254 | A1 | 19980423 | (199822)* | EN | 25[0] | |
| AU 9748079 | A | 19980511 | (199837) | EN | | |
| EP 932417 | A1 | 19990804 | (199935) | EN | | |
| US 6083477 | A | 20000704 | (200036) | EN | | |
| AU 729515 | B | 20010201 | (200112) | EN | | |
| JP 2001503253 | W | 20010313 | (200117) | JA | 29 | |
| US 6399068 | B1 | 20020604 | (200242) | EN | | |
| US 20030031669 | A1 | 20030213 | (200314) | EN | | |
| EP 932417 | B1 | 20030305 | (200318) | EN | | |
| DE 69719529 | E | 20030410 | (200332) | DE | | |
| ES 2191827 | T3 | 20030916 | (200368) | ES | | |
| US 20050175582 | A1 | 20050811 | (200553) | EN | | |
| JP 2006089491 | A | 20060406 | (200625) | JA | 14 | |
| US 7033572 | B2 | 20060425 | (200628) | EN | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 9816254 | A1 | WO 1997-US17924 | 19971014 |
| US 6083477 | A Provisional | US 1996-28430P | 19961017 |
| US 6399068 | B1 Provisional | US 1996-28430P | 19961017 |
| US 20030031669 | A1 Provisional | US 1996-28430P | 19961017 |
| US 20050175582 | A1 Provisional | US 1996-28430P | 19961017 |

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|---|---|
| AU 9748079 A | AU 1997-48079 19971014 |
| AU 729515 B | AU 1997-48079 19971014 |
| DE 69719529 E | DE 1997-619529 19971014 |
| EP 932417 A1 | EP 1997-910793 19971014 |
| EP 932417 B1 | EP 1997-910793 19971014 |
| DE 69719529 E | EP 1997-910793 19971014 |
| ES 2191827 T3 | EP 1997-910793 19971014 |
| US 6083477 A | US 1997-949758 19971014 |
| US 6399068 B1 Div Ex | US 1997-949758 19971014 |
| US 20030031669 A1 Div Ex | US 1997-949758 19971014 |
| US 20050175582 A1 Div Ex | US 1997-949758 19971014 |
| EP 932417 A1 | WO 1997-US17924 19971014 |
| JP 2001503253 W | WO 1997-US17924 19971014 |
| EP 932417 B1 | WO 1997-US17924 19971014 |
| DE 69719529 E | WO 1997-US17924 19971014 |
| JP 2001503253 W | JP 1998-518402 19971014 |
| JP 2006089491 A Div Ex | JP 1998-518402 19971014 |
| US 6399068 B1 | US 2000-599550 20000623 |
| US 20030031669 A1 Div Ex | US 2000-599550 20000623 |
| US 20050175582 A1 Div Ex | US 2000-599550 20000623 |
| US 20030031669 A1 | US 2002-117342 20020408 |
| US 20050175582 A1 Div Ex | US 2002-117342 20020408 |
| US 20050175582 A1 | US 2005-56187 20050214 |
| JP 2006089491 A | JP 2005-292358 20051005 |
| US 7033572 B2 Provisional | US 1996-28430P 19961017 |
| US 7033572 B2 Div Ex | US 1997-949758 19971014 |
| US 7033572 B2 Div Ex | US 2000-599550 20000623 |
| US 7033572 B2 | US 2002-117342 20020408 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO | |
|---|---|---|---|---|
| AU 729515 | B | Previous Publ | AU 9748079 | A |
| DE 69719529 | E | Based on | EP 932417 | A |
| ES 2191827 | T3 | Based on | EP 932417 | A |
| US 6399068 | B1 | Div ex | US 6083477 | A |
| US 20030031669 | A1 | Div ex | US 6083477 | A |
| US 20050175582 | A1 | Div ex | US 6083477 | A |
| US 20030031669 | A1 | Div ex | US 6399068 | B |
| US 20050175582 | A1 | Div ex | US 6399068 | B |
| AU 9748079 | A | Based on | WO 9816254 | A |
| EP 932417 | A1 | Based on | WO 9816254 | A |
| AU 729515 | B | Based on | WO 9816254 | A |
| JP 2001503253 | W | Based on | WO 9816254 | A |
| EP 932417 | B1 | Based on | WO 9816254 | A |
| DE 69719529 | E | Based on | WO 9816254 | A |
| US 7033572 | B2 | Div ex | US 6083477 | A |
| US 7033572 | B2 | Div ex | US 6399068 | B |

PRIORITY APPLN. INFO: US 1996-28430P 19961017
US 1997-949758 19971014
US 2000-599550 20000623
US 2002-117342 20020408
US 2005-56187 20050214

AB WO 1998016254 A1 UPAB: 20060114
A conjugate (A) of a non-immunogenic toxin or therapeutic radionuclide (I) and a cell-specific cytokine (II) is new. Also new is a fusion protein (bispecific antibody) (B), with one specificity for a cell marker specific to malignant cells and another specific for a region of interleukin (IL)-15α. (I) is RNase

or onconase (Ia; an RNase from Rana pipiens oocytes) and (II) is IL-15 (also suitable is IL-2). Where (Ia) is used, (A) also includes a diagnostic radionuclide attached to (II). (B) is a single-strand (sc) Fv, particularly a fusion of two individual Fv. The cell marker is a B-cell related antigen, particularly CD20 (but also CD38 for acute lymphocytic leukaemia or multiple myeloma or CD15 for ALL or chronic myelogenous leukaemia) and the second specificity is the α-chain of the IL-15 receptor, targeting the extracellular domain of IL-15. (B) is used to present the IL-15 receptor on the surface of target cells that already express the β and γ chains, resulting, after administration of (A), in internalisation of the ligand/receptor complex.

USE - Tumours are treated by administering first (B), then (A), optionally in conjunction with chemotherapy and/or radiation therapy to prevent tumour cells from activating DNA repair. Particularly the treatment is applied to B-cell lymphocytic, hairy cell or acute myelogenous leukaemias (AML) or non-Hodgkin's lymphoma.

ADVANTAGE - The value of surface antigens as targets is improved by linkage to a high affinity, internalising receptor system (IL-15α), resulting in increased intracellular delivery of (I) and reduced tendency for the antibody to dissociate rapidly from the cell surface. Both (A) and (B) are only weakly antigenic and can be produced in low molecular weight forms that penetrate well into tumours and clear rapidly from normal tissue.

L70 ANSWER 33 OF 46 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1993-386207 [48] WPIX
CROSS REFERENCE: 1989-294546; 1990-377940; 1991-088800; 1991-353908; 1994-262599; 1994-332836
DOC. NO. CPI: C1993-171704 [48]
TITLE: New stable conjugate of targetting protein with toxin or drug - bound to mercapto gp. in protein and internalised after binding to target cell, for treating tumours and microbial infections
DERWENT CLASS: A96; B04; D16
INVENTOR: GOLDENBERG D M; GRIFFITHS G L; HANSEN H J; LENTINE-JONES A
PATENT ASSIGNEE: (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 17

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| WO 9323062 | A1 | 19931125 | (199348)* | EN | 29[0] | |
| EP 651646 | A1 | 19950510 | (199523) | EN | | |
| US 5541297 | A | 19960730 | (199636) | EN | 7[0] | |
| JP 08500084 | W | 19960109 | (199642) | JA | 33[0] | |
| US 5601825 | A | 19970211 | (199712) | EN | 7[0] | |
| EP 651646 | A4 | 19970709 | (199813) | EN | | |
| CA 2118032 | C | 19980929 | (199849) | EN | | |
| JP 2942356 | B2 | 19990830 | (199941) | JA | 10 | |
| EP 1283059 | A2 | 20030212 | (200312) | EN | | |
| EP 651646 | B1 | 20030903 | (200360) | EN | | |
| DE 69333182 | E | 20031009 | (200374) | DE | | |
| ES 2208639 | T3 | 20040616 | (200442) | ES | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|

| | |
|---|---|
| WO 9323062 A1 | WO 1993-US4136 19930507 |
| US 5541297 A Cont of | US 1988-176421 19880401 |
| US 5601825 A Cont of | US 1988-176421 19880401 |
| US 5541297 A CIP of | US 1989-364373 19890612 |
| US 5601825 A CIP of | US 1989-364373 19890612 |
| US 5541297 A CIP of | US 1989-392280 19890810 |
| US 5601825 A CIP of | US 1989-392280 19890810 |
| US 5541297 A CIP of | US 1989-408241 19890918 |
| US 5601825 A CIP of | US 1989-408241 19890918 |
| US 5541297 A CIP of | US 1990-518707 19900507 |
| US 5601825 A CIP of | US 1990-518707 19900507 |
| US 5541297 A CIP of | US 1990-581913 19900913 |
| US 5601825 A CIP of | US 1990-581913 19900913 |
| US 5541297 A CIP of | US 1991-760466 19910917 |
| US 5601825 A CIP of | US 1991-760466 19910917 |
| US 5541297 A | US 1992-882177 19920511 |
| US 5601825 A Div Ex | US 1992-882177 19920511 |
| CA 2118032 C | CA 1993-2118032 19930507 |
| DE 69333182 E | DE 1993-69333182 19930507 |
| EP 651646 A1 | EP 1993-910988 19930507 |
| EP 651646 A4 | EP 1993-910988 19930507 |
| EP 1283059 A2 Div Ex | EP 1993-910988 19930507 |
| EP 651646 B1 | EP 1993-910988 19930507 |
| DE 69333182 E | EP 1993-910988 19930507 |
| ES 2208639 T3 | EP 1993-910988 19930507 |
| JP 08500084 W | JP 1993-518731 19930507 |
| JP 2942356 B2 | JP 1993-518731 19930507 |
| EP 651646 A1 | WO 1993-US4136 19930507 |
| JP 08500084 W | WO 1993-US4136 19930507 |
| JP 2942356 B2 | WO 1993-US4136 19930507 |
| EP 651646 B1 | WO 1993-US4136 19930507 |
| DE 69333182 E | WO 1993-US4136 19930507 |
| US 5601825 A | US 1995-452131 19950526 |
| EP 1283059 A2 | EP 2002-79619 19930507 |
| EP 651646 B1 Related to | EP 2002-79619 19930507 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| EP 651646 B1 | Related to | EP 1283059 A |
| EP 1283059 A2 | Div ex | EP 651646 A |
| DE 69333182 E | Based on | EP 651646 A |
| ES 2208639 T3 | Based on | EP 651646 A |
| JP 2942356 B2 | Previous Publ | JP 08500084 W |
| US 5541297 A | Cont of | US 5061641 A |
| US 5601825 A | Cont of | US 5061641 A |
| US 5541297 A | CIP of | US 5128119 A |
| US 5601825 A | CIP of | US 5128119 A |
| US 5541297 A | CIP of | US 5328679 A |
| US 5601825 A | CIP of | US 5328699 A |
| US 5601825 A | Div ex | US 5541297 A |
| EP 651646 A1 | Based on | WO 9323062 A |
| JP 08500084 W | Based on | WO 9323062 A |
| JP 2942356 B2 | Based on | WO 9323062 A |
| EP 651646 B1 | Based on | WO 9323062 A |
| DE 69333182 E | Based on | WO 9323062 A |

PRIORITY APPLN. INFO: US 1992-882177 19920511
US 1988-176421 19880401

US 1989-364373 19890612
US 1989-392280 19890810
US 1989-408241 19890918
US 1990-518707 19900507
US 1990-581913 19900913
US 1991-760466 19910917
US 1995-452131 19950526

AB WO 1993023062 A1 UPAB: 20050701
Conjugate (A) comprises (1) a drug or modified toxin (i.e. a native toxin without a functional receptor-binding domain) and (2) a protein (I) which reacts with a component (II) of a targeted cell or pathogenic microbe. (II) internalises (A) into the cell or microbial cytoplasm and, before conjugation, (I) has at least one SH gp. which becomes a site of conjugation.
Pref. (I) is a (poly)peptide, hormone, lymphokine, growth factor, albumin, cytokine, enzyme, immune modulator, receptor protein, or antibody (fragment) and Sh gps. may be introduced by reduction of a disulphide bond. Component (1) is pref. abrin, alpha toxin, diphtheria toxin, exotoxin, gelonin, pokeweed antiviral protein, ricin or saporin, or puromycin, cycloheximide or ribonuclease.
USE/ADVANTAGE - (A) are used to treat cancers (partic. B- cell lymphoma or leukaemia) or infections caused by e.g. viruses (including HIV), protozoa or bacteria. They are admin. parenterally at unit doses of 10-500 mg. By site-specific attachment of the toxin or drug to SH gps., highly immunoreactive conjugates are formed which are stable in blood or other body fluids.

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L70 ANSWER 34 OF 46 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001347219 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11410483
TITLE: Therapy of disseminated B-cell lymphoma xenografts in severe combined immunodeficient mice with an anti-CD74 antibody conjugated with (111)indium, (67)gallium, or (90)yttrium.
AUTHOR: Ochakovskaya R; Osorio L; Goldenberg D M; Mattes M J
CORPORATE SOURCE: Garden State Cancer Center, Belleville, New Jersey 07109, USA.
CONTRACT NUMBER: CA39841 (NCI)
CA87059 (NCI)
SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (2001 Jun) Vol. 7, No. 6, pp. 1505-10.
Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 24 Sep 2001
Last Updated on STN: 24 Sep 2001
Entered Medline: 20 Sep 2001

AB A radiolabeled antibody (Ab) to CD74 (the MHC class II invariant chain, Ii) was shown previously to effectively kill human B-lymphoma cells in vitro. Conjugates with both Auger electron and beta-particle emitters were able to kill cells, but the former displayed less nonspecific toxicity in the in vitro

assay used. In this report, we have extended the studies to an in vivo model of tumor growth. The human B- cell lymphoma Raji was injected i.v. into severe combined immunodeficient mice, and radiolabeled Abs were injected at various times after tumor inoculation. The maximum tolerated dose (MTD), as well as lower doses, was tested. Tumor growth was monitored by hind-leg paralysis. With a 3-5-day interval before Ab injection, anti- CD74 conjugated to either (111)In or (67)Ga, at a dose of 240-350 microCi/mouse, produced a strong therapeutic effect, with greatly delayed tumor growth, and many of the treated mice were tumor free for >6 months. Control mice became paralyzed in 16-24 days, uniformly. Treatment at later time points (9-day interval) had little therapeutic effect. The MTD was required for optimal therapy. With the beta-particle emitter (90)Y, the MTD was much less, 25 microCi/mouse, and at this dose there was only a weak therapeutic effect. In conclusion, the data suggest that low-energy electrons are more effective than beta-particles in this model system. These results may be applicable to humans, particularly in the case of micrometastatic disease. This approach may also be effective with other Abs that accrete in large amounts.

L70 ANSWER 35 OF 46 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2001147663 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11154233
TITLE: Potent and specific antitumor effects of an anti-CD22-targeted cytotoxic ribonuclease: potential for the treatment of non-Hodgkin lymphoma.
AUTHOR: Newton D L; Hansen H J; Mikulski S M; Goldenberg D M; Rybak S M
CORPORATE SOURCE: SAIC Frederick, National Cancer Institute-Frederick Cancer Research and Development Center, Frederick, MD 21702-1201, USA.
CONTRACT NUMBER: CA39841 (NCI)
N01-CO-56000 (NCI)
SOURCE: Blood, (2001 Jan 15) Vol. 97, No. 2, pp. 528-35.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 4 Apr 2001
Last Updated on STN: 11 Dec 2002
Entered Medline: 15 Mar 2001

AB LL2, an anti-CD22 monoclonal antibody against B-cell lymphoma, was covalently linked to the amphibian ribonuclease, onconase, a member of the pancreatic RNase A superfamily. LL2 increased in vitro potency (10 000-fold) and specificity against human Daudi Burkitt lymphoma cells while decreasing systemic toxicity of onconase. Monensin further increased potency of LL2-onconase on Daudi cells (IC(50), 20 and 1.5 pM, absence and presence of monensin, respectively). A 1-hour exposure to LL2-onconase was sufficient to kill Daudi cells in culture. These favorable in vitro properties translated to significant antitumor activity against disseminated Daudi lymphoma in mice with severe combined immunodeficiency disease. In mice inoculated with tumor cells intraperitoneally (ip), LL2-onconase (100 microg 5 times ip every day) increased the life span of animals with minimal disease 200%. The life span of mice with advanced disseminated Daudi lymphoma (tumor cells inoculated intravenously) was increased 135%. Mice injected with LL2-onconase tolerated a dose as high as 300 mg/kg. Because both onconase and LL2 are in clinical trials as cancer therapeutics, the covalently linked agents should be considered for treatment of non-Hodgkin lymphoma.

L70 ANSWER 36 OF 46 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002022231 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11418304
TITLE: Specifically targeting the CD22 receptor of human B -cell lymphomas with RNA damaging agents.
AUTHOR: Newton D L; Hansen H J; Liu H; Ruby D; Iordanov M S; Magun B E; Goldenberg D M; Rybak S M
CORPORATE SOURCE: SAIC Frederick, National Cancer Institute-Frederick Cancer Research and Development Center, Room 162, Building 567, Frederick, MD 21702-1201, USA.
CONTRACT NUMBER: CA-39360 (NCI)
ES-08456 (NIEHS)
N01-CO-56000 (NCI)
SOURCE: Critical reviews in oncology/hematology, (2001 Jul-Aug) Vol. 39, No. 1-2, pp. 79-86. Ref: 59
Journal code: 8916049. ISSN: 1040-8428.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 21 Jan 2002
Last Updated on STN: 21 Jan 2002
Entered Medline: 14 Dec 2001

AB Targeting CD22 on human B-cells with a monoclonal antibody conjugated to a cytotoxic RNAse causes potent and specific killing of the lymphoma cells in vitro. This translates to anti-tumor effects in human lymphoma models in SCID mice. RNA damage caused by RNAses could be an important alternative to standard DNA damaging chemotherapeutics. Moreover, targeted RNAses may overcome problems of toxicity and immunogenicity associated with plant or bacterial toxin containing immunotoxins.

L70 ANSWER 37 OF 46 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2000418700 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10941903
TITLE: Localization of an antibody to CD74 (MHC class II invariant chain) to human B cell lymphoma xenografts in nude mice.
AUTHOR: Shih L; Ong G L; Burton J; Mishina D; Goldenberg D M; Mattes M J
CORPORATE SOURCE: Garden State Cancer Center, Belleville, NJ 07109, USA.
CONTRACT NUMBER: CA39481 (NCI)
SOURCE: Cancer immunology, immunotherapy : CII, (2000 Jul) Vol. 49, No. 4-5, pp. 208-16.
Journal code: 8605732. ISSN: 0340-7004.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 15 Sep 2000
Last Updated on STN: 15 Sep 2000
Entered Medline: 5 Sep 2000

AB The tumor-specific localization of an anti-CD74 Ab, LL1, was demonstrated in nude mice bearing xenografts of human B -cell lymphoma. This Ab, conjugated to radionuclides emitting Auger electrons, including 125I and 111In, was previously reported to kill tumor cells in vitro effectively and specifically. The cytotoxic potency of this Ab is due to its uptake and catabolism at a very high level, which also affected the Ab biodistribution experiments. Thus, Ab localization to the tumor was only detected if a "residualizing" radiolabel was used, meaning a label that is trapped within cells, usually within lysosomes, after catabolism of the Ab to which it was conjugated. Similar results were obtained with three different residualizing labels: 111In conjugated via the chelators benzyl diethylenetriaminepentaacetic acid (DTPA) or 1.4,7,10-tetra-azacyclododecane-N, N', N", N"'-tetraacetic acid (DOTA), or 131I-dilactitol-tyramine, a residualizing form of iodine. The Ab protein dose could be high, 0.5 mg/mouse, without causing a decrease in specific tumor uptake, probably reflecting the high capacity for uptake. Moreover, tumors of moderate size were found to cause rapid, specific removal of the Ab from the blood, also a result of catabolic processes. This induced blood clearance naturally affected the Ab localization experiments, but this factor could be circumvented by increasing the Ab protein dose. Using a different Ab, anti-(mature MHC class II), the ability of Ab to penetrate relatively large solid tumors was investigated. Complete saturation of antigenic sites was observed in tumors up to 0.3 g in size, but quite high Ab protein doses were required, 5.0 mg/ mouse. These results provide a rationale for attempting therapy with radiolabeled LL1.

L70 ANSWER 38 OF 46 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 93153779 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8428363
TITLE: Pseudomonas exotoxin-based immunotoxins containing the antibody LL2 or LL2-Fab' induce regression of subcutaneous human B-cell lymphoma in mice.
AUTHOR: Kreitman R J; Hansen H J; Jones A L; FitzGerald D J; Goldenberg D M; Pastan I
CORPORATE SOURCE: Laboratory of Molecular Biology, National Cancer Institute, NIH, Bethesda, Maryland 20892.
CONTRACT NUMBER: CA39841 (NCI)
SOURCE: Cancer research, (1993 Feb 15) Vol. 53, No. 4, pp. 819-25.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199303
ENTRY DATE: Entered STN: 26 Mar 1993
Last Updated on STN: 20 Apr 2002
Entered Medline: 10 Mar 1993

AB We have produced immunotoxins using LL2, a monoclonal antibody which binds to human B-cell lymphomas and which, in a radioiodinated form, induced responses in lymphoma patients (D.M. Goldberg et al., J. Clin. Oncol., 9: 548-564, 1991). We have coupled LL2 to Lys-PE38KDEL, a derivative of Pseudomonas exotoxin (PE) which does not bind to the PE receptor. LL2-PE38KDEL was cytotoxic toward several Burkitt's lymphoma lines, with 50% inhibitory concentration values ranging from 2 to 6 ng/ml (10-30 pM). Another immunotoxin, LL2-Fab'-PE38KDEL, was produced by chemically coupling the Fab' fragment of LL2 to Lys-PE38KDEL. LL2-Fab'-PE38KDEL also was cytotoxic toward the Burkitt's cells, with a 50% inhibitory concentration of 1-2 ng/ml (13-24 PM). The antibody LL2 alone had no cytotoxicity toward the malignant cells,

and excess LL2 prevented the cytotoxicity of LL2-PE38KDEL and LL2-Fab'-PE38KDEL. Control immunotoxins UPC-10-PE38KDEL and Mu-9-Fab'-PE38KDEL were not cytotoxic. LL2-PE38KDEL and LL2-Fab'-PE38KDEL bound to cells with 50% and 17% of the affinity of LL2, respectively. Both immunotoxins, but not UPC-10-PE38KDEL, prevented the development of CA-46 tumors in nude mice. LL2-PE38KDEL and LL2-Fab'-PE38KDEL, but not the control immunotoxins, led to complete regressions of measurable s.c. CA-46 tumors in nude mice, when given at 50% and 35% of the 50% lethal dose, respectively. LL2 alone significantly retarded the growth of CA-46 tumors but did not cause complete tumor regressions. Immunotoxins containing derivatives of Pseudomonas exotoxin can be targeted to human B-cell lymphoma and merit further study as potential therapeutic agents.

L70 ANSWER 39 OF 46 MEDLINE on STN
ACCESSION NUMBER: 2000007392 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10541379
TITLE: Low- versus high-dose radioimmunotherapy with humanized anti-CD22 or chimeric anti-CD20 antibodies in a broad spectrum of B cell -associated malignancies.
AUTHOR: Behr T M; Wormann B; Gramatzki M; Riggert J; Gratz S; Behe M; Griesinger F; Sharkey R M; Kolb H J; Hiddemann W; Goldenberg D M; Becker W
CORPORATE SOURCE: Department of Nuclear Medicine, Georg-August-University of Gottingen, Germany.. tmbehr@med.uni-goettingen.de
CONTRACT NUMBER: CA 39841 (NCI)
SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (1999 Oct) Vol. 5, No. 10 Suppl, pp. 3304s-3314s. Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 11 Jan 2000
Last Updated on STN: 11 Jan 2000
Entered Medline: 24 Nov 1999

AB Both CD22 and CD20 have been used successfully as target molecules for radioimmunotherapy (RAIT) of low-grade B cell non-Hodgkin's lymphoma. Because both CD20 and CD22 are highly expressed relatively early in the course of B cell maturation, and because its expression is maintained up to relatively mature stages, we studied the potential of the humanized anti-CD22 antibody, hLL2, as well as of the chimeric anti-CD20 (chCD20) antibody, rituximab (IDEC-C2B8), for low- or high-dose (myeloablative) RAIT of a broad range of B cell-associated hematological malignancies. A total of 10 patients with chemorefractory malignant neoplasms of B cell origin were studied with diagnostic (n = 5) and/or potentially therapeutic doses (n = 9) of hLL2 (n = 4; 0.5 mg/kg, 8-315 mCi of 131I) or chCD20 (n = 5; 2.5 mg/kg, 15-495 mCi of 131I). The diagnostic doses were given to establish the patients' eligibility for RAIT and to estimate the individual radiation dosimetry. One patient suffered of Waldenstrom's macroglobulinemia, eight patients had low- (n = 4), intermediate- (n = 2) or high- (n = 2) grade non-Hodgkin's lymphoma, and one patient had a chemorefractory acute lymphatic leukemia, after having failed five heterologous bone marrow or stem cell transplantations. Three of these 10 patients were scheduled for treatment with conventional (30-63 mCi, cumulated doses of up to 90 mCi of 131I) and 7 with potentially myeloablative

(225-495 mCi of 131I) activities of 131I-labeled hLL2 or chCD20 (0.5 and 2.5 mg/kg, respectively); homologous (n = 6) or heterologous (n = 1) stem cell support was provided in these cases. Good tumor targeting was observed in all diagnostic as well as posttherapeutic scans of all patients. In myeloablative therapies, the therapeutic activities were calculated based on the diagnostic radiation dosimetry, aiming at lung and kidney doses < or = 20 Gy. Stem cells were reinfused when the whole-body activity retention fell below 20 mCi. In eight assessable patients, five had complete remissions, two experienced partial remissions (corresponding to an overall response rate of 87%), and one (low-dose) patient had progressive disease despite therapy. In the five assessable, actually stem-cell grafted patients, the complete response rate was 100%. Both CD20 and CD22 seem to be suitable target molecules for high-dose RAIT in a broad spectrum of hematological malignancies of B cell origin with a broad range of maturation stages (from acute lymphatic leukemia to Waldenstrom's macroglobulinemia). The better therapeutic outcome of patients undergoing high-dose, myeloablative RAIT favors this treatment concept over conventional, low-dose regimens.

L70 ANSWER 40 OF 46 MEDLINE on STN
ACCESSION NUMBER: 96075434 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7493380
TITLE: Development and evaluation of the specificity of a rat monoclonal anti-idiotype antibody, WN, to an anti-B -cell lymphoma monoclonal antibody, LL2.
AUTHOR: Losman M J; Leung S O; Shih L B; Shevitz J; Shukla R; Haraga L; Goldenberg D M; Hansen H J
CORPORATE SOURCE: Immunomedics, Inc., Morris Plains, New Jersey 07950, USA.
CONTRACT NUMBER: CA 39841 (NCI)
SOURCE: Cancer research, (1995 Dec 1) Vol. 55, No. 23 Suppl, pp. 5978s-5982s.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 17 Feb 1996
Last Updated on STN: 17 Feb 1996
Entered Medline: 11 Jan 1996

AB Anti-idiotype monoclonal antibodies (Mabs) to mLL2, an anti-B- cell lymphoma and CD22-specific murine IgG2a-kappa Mab, were generated by hybridoma technology from splenocytes of Copenhagen rats immunized with mLL2 F(ab')2. Mab WN, an IgG2a-kappa, was selected based on its specific binding to mLL2 and not other IgG isotypes or anti- B-cell Mabs. In a radioimmunoassay, WN was found to inhibit the binding of 125I-labeled mLL2 to Raji cells and to have no effect on the binding of other B-cell-reactive antibodies. Using high performance liquid chromatography analysis, WN was shown to complex specifically with both mLL2 and mLL2 Fab'. Meanwhile, we have constructed chimeric (cLL2) and humanized (hLL2) versions of LL2. Both cLL2 and hLL2 were demonstrated to retain the original antigen specificity and affinity of mLL2 [S.O. Leung et al., Proc. Am. Associate Cancer Res., 2872 (abstract), 34: 481, 1993]. The specific binding of WN to either radioiodinated or peroxidase-conjugated mLL2 was inhibited in a dose-response manner, and to a similar extent by mLL2, cLL2, and hLL2. Since the mLL2 complementarity-determining regions are the only sequences common to mLL2, cLL2, and hLL2, the result confirms that WN is specific to the antigen-binding complementarity-determining regions. A WN binding assay is currently being evaluated as a substitute for the tedious, and sometimes inconsistent, Raji cell-binding

assay for the determination of LL2 immunoreactivity. In conclusion, we have developed an anti-idiotype Mab, WN, to mLL2. Its potential use as a surrogate antigen for B -cell lymphoma is under investigation.

L70 ANSWER 41 OF 46 MEDLINE on STN
ACCESSION NUMBER: 96256892 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8643111
TITLE: Construction and characterization of a humanized, internalizing, B-cell (CD22)-specific, leukemia/lymphoma antibody, LL2.
AUTHOR: Leung S O; Goldenberg D M; Dion A S; Pellegrini M C; Shevitz J; Shih L B; Hansen H J
CORPORATE SOURCE: Immunomedics, Inc., Morris Plains, NJ 07950, USA.
CONTRACT NUMBER: CA 39841 (NCI)
SOURCE: Molecular immunology, (1995 Dec) Vol. 32, No. 17-18, pp. 1413-27.
Journal code: 7905289. ISSN: 0161-5890.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1REI; PDB-3FAB
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 26 Jul 1996
Last Updated on STN: 3 Feb 1997
Entered Medline: 15 Jul 1996

AB The murine monoclonal antibody, LL2, is a B-cell (CD22)-specific IgG2a which has been demonstrated to be clinically significant in the radioimmunodetection of non-Hodgkin's B- cell lymphoma. The antibody carries a variable region-appended glycosylation site in the light chain and is rapidly internalized upon binding to Raji target cells. Humanization of LL2 was carried out in order to develop LL2 as a diagnostic and immunotherapeutic suitable for repeated administration. Based on the extent of sequence homology, and with the aid of computer modeling, we selected the EU framework regions (FR) 1, 2 and 3, and the NEWM FR4 as the scaffold for grafting the heavy chain complementarity determining regions (CDRs), and REI FRs for that of light chains. The light chain glycosylation site, however, was not included. Construction of the CDR-grafted variable regions was accomplished by a rapid and simplified method that involved long DNA oligonucleotide synthesis and the polymerase chain reaction (PCR). The humanized LL2 (hLL2), lacking light chain variable region glycosylation, exhibited immunoreactivities that were comparable to that of chimeric LL2 (cLL2), which was shown previously to have antigen-binding properties similar to its murine counterpart, suggesting that the VK-appended oligosaccharides found in mLL2 are not necessary for antigen binding. Moreover, the hLL2 retained its ability to be internalized into Raji cells at a rate similar to its murine and chimeric counterparts.

L70 ANSWER 42 OF 46 MEDLINE on STN
ACCESSION NUMBER: 95130289 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7829269
TITLE: Effect of VK framework-1 glycosylation on the binding affinity of lymphoma-specific murine and chimeric LL2 antibodies and its potential use as a novel conjugation site.
AUTHOR: Leung S O; Dion A S; Pellegrini M C; Losman M J; Grebenau R C; Goldenberg D M; Hansen H J
CORPORATE SOURCE: Immunomedics, Inc., Morris Plains, NJ 07950.

CONTRACT NUMBER: CA 39841 (NCI)
SOURCE: International journal of cancer. Journal international du cancer, (1995 Feb 8) Vol. 60, No. 4, pp. 534-8.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 7 Mar 1995
Last Updated on STN: 7 Mar 1995
Entered Medline: 22 Feb 1995

AB A potential asparagine (Asn)-linked glycosylation site was identified in the VK FRI sequence of an anti-B lymphoma monoclonal antibody (MAb), LL2.SDS-PAGE analysis and endo-F treatment of both murine and chimeric LL2 antibodies indicated that this site was glycosylated; however, no differences in the binding affinity to Raji cells were observed between the native murine LL2 and the endo-F-deglycosylated murine LL2 antibodies. Elimination of the glycosylation site from the chimeric LL2 antibody was accomplished by an Asn to Gln mutation in the tri-acceptor site found in the light chain. The resultant aglycosylated chimeric LL2 exhibited a similar Raji cell binding affinity to that of the glycosylated form. The results are in agreement with computer modeling studies which suggested the lack of interactions between the oligosaccharide moiety and the CDRs. The finding is interesting because it enables a wider choice of human framework sequences, which in most cases do not have a corresponding glycosylation site, for the humanization of the LL2 VK domain, as well as a greater latitude of host expression systems. Most importantly, the LL2 VK carbohydrate moiety might be used as a novel conjugation site for drugs and radionuclides without compromising the immunoreactivity of the antibody.

L70 ANSWER 43 OF 46 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 5
ACCESSION NUMBER: 1998:196835 BIOSIS Full-text
DOCUMENT NUMBER: PREV199800196835
TITLE: In vitro and in vivo characterization of LL2-RNase conjugates against the CD22 antigen on human B-cell lymphomas.
AUTHOR(S): Newton, D. L. [Reprint author]; Hansen, H. J.; Mikulski, S. M.; Goldenberg, D. M.; Rybak, S. M.
CORPORATE SOURCE: Natl. Cancer Inst., Frederick, MD 21702, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1998) Vol. 39, pp. 435. print.
Meeting Info.: 89th Annual Meeting of the American Association for Cancer Research. New Orleans, Louisiana, USA. March 28-April 1, 1998. American Association for Cancer Research.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 May 1998
Last Updated on STN: 4 May 1998

L70 ANSWER 44 OF 46 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:187834 BIOSIS Full-text

DOCUMENT NUMBER: PREV199598202134
TITLE: Characteristics of surviving leukocytes following experimental radioimmunotherapy (RAIT).
AUTHOR(S): Blumenthal, R. D. [Reprint author]; Hess, J.; Sharkey, R. M.; Palermo, C.; Goldenberg, D. M.
CORPORATE SOURCE: Garden State Cancer Cent., Newark, NJ 07103, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (1995) Vol. 36, No. 0, pp. 615.
Meeting Info.: Eighty-sixth Annual Meeting of the American Association for Cancer Research. Toronto, Ontario, Canada. March 18-22, 1995.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1995
Last Updated on STN: 9 Jun 1995

L70 ANSWER 45 OF 46 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2002160736 EMBASE Full-text
TITLE: Specifically targeting the CD22 receptor of human B-cell lymphomas with RNA damaging agents: A new generation of therapeutics.
AUTHOR: Hursey M.; Newton D.L.; Hansen H.J.; Ruby D.; Goldenberg D.M.; Rybak S.M.
CORPORATE SOURCE: S.M. Rybak, Developmental Therapeutics Program, Natl. Cancer Institute-Frederick, Cancer Research/Development Center, Frederick, MD 21702-1201, United States. rybak@ncifcrf.gov
SOURCE: Leukemia and Lymphoma, (2002) Vol. 43, No. 5, pp. 953-959.
.
Refs: 47
ISSN: 1042-8194 CODEN: LELYEA
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 May 2002
Last Updated on STN: 16 May 2002

AB Targeting CD22 on human B-cells with a monoclonal antibody conjugated to a cytotoxic RNAse causes potent and specific killing of the lymphoma cells in vitro. This translates to anti-tumor effects in human lymphoma models in SCID mice. RNA damage caused by RNAses could be an important alternative to standard DNA-damaging chemotherapeutics. A second generation construct with an improved recombinant cytotoxic RNAse is described. Targeted RNAses may overcome problems of toxicity and immunogenicity associated with plant or bacterial toxin-containing immunoconjugates.

L70 ANSWER 46 OF 46 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-28629 DRUGU B P S Full-text
TITLE: Targeted apoptosis: RNA damaging agents linked to antibodies.
AUTHOR: Rybak S; Newton D L N; Hansen H J; Goldenberg D M

CORPORATE SOURCE: Nat.Cancer-Inst.Frederick
LOCATION: Frederick, Md., USA
SOURCE: Cancer Biother.Radiopharm. (17, No. 4, 473-74, 2002)
CODEN: CBRAF ISSN: 1084-9785
AVAIL. OF DOC.: National Cancer Institute, Frederick, MD, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB The targeting of the recombinant RNase onconase (p-30) to tumor cells by linking to LL2 anti-CD22 MAb against B -cell lymphoma is reported. The potency of onconase against Daudi Burkitt's lymphoma cells in-vitro was increased 10000-fold, and in-vivo toxicity was reduced. Antitumor activity was demonstrated in SCID mice bearing Daudi lymphoma at 2.5 mg/kg, and mice tolerated a dose of 600 mg/kg. RNase conjugates are being evaluated in epithelial cancer. (conference abstract: Ninth Conference on Cancer Therapy with Antibodies and Immunoconjugates, Princeton, New Jersey, October 24-26, 2002). (No EX).

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=> d his nofile

     (FILE 'HOME' ENTERED AT 16:10:55 ON 10 JUL 2007)

     FILE 'HCAPLUS' ENTERED AT 16:11:05 ON 10 JUL 2007
L1             2 SEA ABB=ON  PLU=ON  US20020041847/PN
                 D TI 1-2
                 D L1 1 ALL

     FILE 'STNGUIDE' ENTERED AT 16:12:45 ON 10 JUL 2007

     FILE 'HCAPLUS' ENTERED AT 16:13:50 ON 10 JUL 2007
                 SEL RN

     FILE 'REGISTRY' ENTERED AT 16:14:05 ON 10 JUL 2007
L2            27 SEA ABB=ON  PLU=ON  (10043-66-0/BI OR 10098-91-6/BI OR
                 23214-92-8/BI OR 50-18-0/BI OR 57-22-7/BI OR 10043-49-9/BI OR
                 11056-06-7/BI OR 14265-85-1/BI OR 14378-26-8/BI OR 14596-37-3/B
                 I OR 14998-63-1/BI OR 154-93-8/BI OR 15755-17-6/BI OR 15755-39-
                 2/BI OR 15757-86-5/BI OR 15776-20-2/BI OR 33419-42-0/BI OR
                 4346-18-3/BI OR 50-02-2/BI OR 50-24-8/BI OR 53-03-2/BI OR
                 58-05-9/BI OR 59-05-2/BI OR 671-16-9/BI OR 83314-01-6/BI OR
                 83869-56-1/BI OR 9001-99-4/BI)

     FILE 'STNGUIDE' ENTERED AT 16:15:25 ON 10 JUL 2007

     FILE 'ZCAPLUS' ENTERED AT 16:19:50 ON 10 JUL 2007
L3               QUE ABB=ON  PLU=ON  B CELL OR T CELL OR MYELOID CELL OR MAST
                 CELL OR PLASMA CELL
L4               QUE ABB=ON  PLU=ON  (ANTIGENS (2A) (CD20 OR CD(W)20)) OR (ANTI
                 (2A)(CD20 OR CD(W)20))
L5               QUE ABB=ON  PLU=ON  (ANTIGENS (2A) (CD74 OR CD 74)) OR (ANTI
                 (2A) (CD74 OR CD(W)74))
L6               QUE ABB=ON  PLU=ON  (HLA DR (2A) ANTIGENS) OR HDA DR
L7               QUE ABB=ON  PLU=ON  NAKED ANTIBODIES OR NAKED ANTIBODY
L8               QUE ABB=ON  PLU=ON  SHEEP OR GOAT OR HORSE OR CATTLE OR ALPACA
                 OR PIG OR DOG OR CAT
L9               QUE ABB=ON  PLU=ON  RADIOLABEL? IMMUNOCONJUGATE?
L10              QUE ABB=ON  PLU=ON  CYTOKINE OR TOXIN OR FUSION PROTEIN OR
                 RNASE OR RECOMBIN? RNASE OR RIBONUCLEASES
L11              QUE ABB=ON  PLU=ON  IMMUNOTHERAP?
L12              QUE ABB=ON  PLU=ON  AUTOIMMUNE DISORDER?
L13              QUE ABB=ON  PLU=ON  (DOMESTIC OR COMPANION) (2A) (ANIMAL)

     FILE 'HCAPLUS' ENTERED AT 16:31:23 ON 10 JUL 2007
L14         139742 SEA ABB=ON  PLU=ON  L2
L15             13 SEA ABB=ON  PLU=ON  RADIOLABEL? IMMUNOCONJUGATE?/OBI
L16         256904 SEA ABB=ON  PLU=ON  CYTOKINE/OBI OR TOXIN/OBI OR FUSION
                 PROTEIN/OBI OR RNASE/OBI OR RECOMBIN? RNASE/OBI OR RIBONUCLEASE
                 S/OBI
L17         374269 SEA ABB=ON  PLU=ON  (L14 OR L15 OR L16)
L18           7247 SEA ABB=ON  PLU=ON  (L4 OR L5 OR L6 OR L7)
L19         204919 SEA ABB=ON  PLU=ON  B CELL/OBI OR T CELL/OBI OR MYELOID
                 CELL/OBI OR MAST CELL/OBI OR PLASMA CELL/OBI
L20         316123 SEA ABB=ON  PLU=ON  SHEEP/OBI OR GOAT/OBI OR HORSE/OBI OR
                 CATTLE/OBI OR ALPACA/OBI OR PIG/OBI OR DOG/OBI OR CAT/OBI
L21           1953 SEA ABB=ON  PLU=ON  L19 (L) L20
L22            286 SEA ABB=ON  PLU=ON  L21 AND (L17 OR L18)
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L23       761994 SEA ABB=ON  PLU=ON  15/SX,SC
L24          248 SEA ABB=ON  PLU=ON  L22 AND L23
L25            9 SEA ABB=ON  PLU=ON  L24 AND L11

     FILE 'ZCAPLUS' ENTERED AT 16:39:44 ON 10 JUL 2007
L26              QUE ABB=ON  PLU=ON  B CELL
L27              QUE ABB=ON  PLU=ON  AY<2003 OR PY<2003 OR PRY<2003
L28              QUE ABB=ON  PLU=ON  AY<2003 OR PRY<2003 OR PY<2003 OR MY<2003
                 OR REVIEW/DT

     FILE 'HCAPLUS' ENTERED AT 16:42:06 ON 10 JUL 2007
L29          185 SEA ABB=ON  PLU=ON  L24 AND L28
L30           49 SEA ABB=ON  PLU=ON  L24 AND L26
L31            0 SEA ABB=ON  PLU=ON  L30 AND L1
L32           39 SEA ABB=ON  PLU=ON  L30 AND L28
L33            3 SEA ABB=ON  PLU=ON  L32 AND L14
L34            3 SEA ABB=ON  PLU=ON  L32 AND L11
L35            0 SEA ABB=ON  PLU=ON  L32 AND L12
L36           10 SEA ABB=ON  PLU=ON  L25 OR L33 OR L34
                 D SCAN

     FILE 'STNGUIDE' ENTERED AT 16:47:19 ON 10 JUL 2007

     FILE 'HCAPLUS' ENTERED AT 16:50:26 ON 10 JUL 2007
                 SAVE TEMP L36 HAR290HCAPAB/A
                 E GOLDENBERG D/AU
L37           52 SEA ABB=ON  PLU=ON  ("GOLDENBERG D"/AU OR "GOLDENBERG D M"/AU)

L38            0 SEA ABB=ON  PLU=ON  L37 AND L1
L39           43 SEA ABB=ON  PLU=ON  GOLDENBERG D M/AU
L40            0 SEA ABB=ON  PLU=ON  L39 AND L1
L41           14 SEA ABB=ON  PLU=ON  (L39 OR L37) AND (L14 OR L17 OR L18)
L42           11 SEA ABB=ON  PLU=ON  L41 AND L28
                 D AU 1-5
                 D TI 1-5
                 SAVE TEMP L42 HAR290HCAPIN/A

     FILE 'WPIX' ENTERED AT 16:56:33 ON 10 JUL 2007
L43          339 SEA ABB=ON  PLU=ON  L21 AND (L17 OR L18)
L44           19 SEA ABB=ON  PLU=ON  L43 AND L11
L45            1 SEA ABB=ON  PLU=ON  L43 AND L1
L46            9 SEA ABB=ON  PLU=ON  L44 AND L27
L47           82 SEA ABB=ON  PLU=ON  GOLDENBERG D M/AU
L48           59 SEA ABB=ON  PLU=ON  L47 AND (L14 OR L17 OR L18)
L49            4 SEA ABB=ON  PLU=ON  L48 AND L12
L50           22 SEA ABB=ON  PLU=ON  L48 AND L26
L51           22 SEA ABB=ON  PLU=ON  L49 OR L50
                 D L51 IN TI 1-5
                 SAVE TEMP L51 HAR290WPIXIN/A

     FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, DRUGU, PASCAL' ENTERED AT
     17:04:51 ON 10 JUL 2007
L52         4293 SEA ABB=ON  PLU=ON  L22
L53          164 SEA ABB=ON  PLU=ON  L52 AND L11
L54            0 SEA ABB=ON  PLU=ON  L53 AND L12
L55          164 SEA ABB=ON  PLU=ON  L53 AND (L8 OR L13)
L56           21 SEA ABB=ON  PLU=ON  L55 AND L26
                 D TI HIT
                 D HIT 2-6
L57           19 SEA ABB=ON  PLU=ON  L56 AND L28
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                SAVE TEMP L57 HAR290MULTI/A
L58          1970 SEA ABB=ON  PLU=ON  L39
L59           408 SEA ABB=ON  PLU=ON  L58 AND (L14 OR L17 OR L18)
L60             0 SEA ABB=ON  PLU=ON  L59 AND L12
L61             0 SEA ABB=ON  PLU=ON  L59 AND L13
                D AU 1-5 L59
L62            78 SEA ABB=ON  PLU=ON  L59 AND L26
L63            22 SEA ABB=ON  PLU=ON  L62 AND ((L5 OR L6 OR L7))
L64            18 SEA ABB=ON  PLU=ON  L62 AND ((L9 OR L10))
L65            38 SEA ABB=ON  PLU=ON  L63 OR L64
L66            21 SEA ABB=ON  PLU=ON  L65 AND L28
L67            21 SEA ABB=ON  PLU=ON  L66 NOT L57
                SAVE TEMP L67 HAR290MULTIN/A

     FILE 'WPIX' ENTERED AT 17:26:42 ON 10 JUL 2007
L68            22 SEA ABB=ON  PLU=ON  L51 NOT L46

     FILE 'STNGUIDE' ENTERED AT 17:27:03 ON 10 JUL 2007
                D QUE L36
                D QUE L46
                D QUE L57

     FILE 'HCAPLUS, WPIX, MEDLINE, BIOSIS, EMBASE, LIFESCI, DRUGU' ENTERED AT
     17:29:31 ON 10 JUL 2007
L69            32 DUP REM L36 L46 L57 (6 DUPLICATES REMOVED)
                     ANSWERS '1-10' FROM FILE HCAPLUS
                     ANSWERS '11-19' FROM FILE WPIX
                     ANSWERS '20-26' FROM FILE MEDLINE
                     ANSWERS '27-28' FROM FILE BIOSIS
                     ANSWER '29' FROM FILE EMBASE
                     ANSWERS '30-32' FROM FILE DRUGU
                D L69 1-10 IBIB ED ABS HITIND
                D L69 11-19 IALL ABEQ TECH ABEX
                D L69 20-32 IBIB AB IND
                D QUE L42
                D QUE L51
                D QUE L67
L70            46 DUP REM L42 L51 L67 (8 DUPLICATES REMOVED)
                     ANSWERS '1-11' FROM FILE HCAPLUS
                     ANSWERS '12-33' FROM FILE WPIX
                     ANSWERS '34-42' FROM FILE MEDLINE
                     ANSWERS '43-44' FROM FILE BIOSIS
                     ANSWER '45' FROM FILE EMBASE
                     ANSWER '46' FROM FILE DRUGU
                D L70 1-11 IBIB AB
                D L70 1 IBIB AB
                D L70 12 BIB AB
                D L70 13-33 IBIB AB
                D L70 34-46 IBIB AB
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